

TROPICAL DISEASES BULLETIN

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THE ANALYSIS OF THE SPOROZOITE RATE

by

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Introduction

The author has tried in previous papers (MACDONALD 1950*a* and *b*) to analyse the effect of a constant inoculation rate on the infection rate. The analysis was confined to those diseases which are characterized by the possibility of super-infection, and was extended to a study of malaria parasite rates in infants. The inoculation rate is not, however, a static and independent factor but is at least partially dependent on the infection rate, and the second essential aspect of a numerical study of epidemiology is the effect of a static infection rate on the inoculation rate. The subject will be studied in the special context of the sporozoite rate in malaria, though the basic theory is equally applicable to insect infectivity rates in all insect-borne diseases.

The sporozoite rate in human malaria is the percentage of anophelines of a given species harbouring sporozoites in their salivary glands. Though it is

commonly equated with the percentage of mosquitoes which are infective to man, JAMES (1931) and others engaged in the deliberate transmission of malaria have shown that the two are by no means identical. It is very commonly measured in field survey and the direct object of malaria control by imagocides is its reduction to negligible levels. Though there have been mathematical workings on its constitution it is curious that there is no generally accepted basis of theory or observation relating it to the factors on which it must depend, and showing how it would be expected to vary with changes in these factors.

The immediate object of the present study is to create such a theory. The factors affecting the rate are first considered and they are then brought together into a general relation expressed as a formula. As a matter of convenience in mathematical working the rate will be referred to as a proportion, which must be multiplied to 100 if conversion to a percentage is desired.

Susceptibility of the Mosquito to Infection

BOYD (1949) has made a full review of the literature on this subject from which, and other sources, the conclusions which follow are drawn. Since many of them are generally accepted, they are not substantiated by reference unless there is particular point in doing so.

1. The susceptibility of different anopheline species varies, though the variation is not as great as might be expected from known differences in their importance in nature. At one time variation was doubted, but precise comparative technique has established it as a fact. BOYD and STRATMAN-THOMAS (1934) showed a material difference in the susceptibilities of *Anopheles quadrimaculatus* and *A. crucians* to *Plasmodium falciparum* infection, in the ratio of 64 to 15 per cent. of successful infections. BOYD and EARLE (1939) showed an even greater difference between *A. quadrimaculatus* and *A. pseudopunctipennis*, of which 79 and 4 per cent. respectively are infected when fed on blood containing Mexican strains of *P. falciparum*, but within the group of notorious vectors there is not much ground for suspecting that major variations such as this are common.

2. Within one species there may be strains which are more susceptible than others, and they may be genetically distinct. This was postulated by HUFF (1931) on a background of experiment with *Culex quinquefasciatus* [*fatigans*] and *Plasmodium cathemerium*. BOYD and RUSSELL (1943) were unable to trace such genetic strains of *A. quadrimaculatus* varying in their susceptibility, but it is now reported (ROCKEFELLER FOUNDATION, 1951) that they have been successfully separated.

3. A species, or perhaps strains within it, may be more susceptible to infection with one species of parasite than with another. As examples, *A. crucians* seems more susceptible to *P. falciparum* than to *P. vivax* (BOYD and STRATMAN-THOMAS, 1934), and *A. sacharovi* shows a similar difference (KLIGLER and MER, 1937).

4. This specificity extends to strains of parasite as well as species. JAMES, NICOL and SHUTE (1932), and SHUTE (1940), in experiments with *A. maculipennis atroparvus*, have shown that it is refractory to infection with Indian and African strains of *P. falciparum*, though susceptible to Roman, Sardinian and Rumanian strains.

5. Superinfection of the mosquito is possible, and available data support the belief that the probability of infecting an anopheline is related to the number of opportunities it has had of feeding on infective persons. The figures given by DANIELS (1901), MITZMAIN (1917) and BOYD (1949, p. 630) support this statement; JAMES (1926) concurs, and the figures given by BARBER (1918),

who did not accept the contention, do not diverge more than is explicable by the errors of sampling.

6. A mosquito which has once become infective remains so for some time but not necessarily for life. The number of sporozoites in the glands is depleted by repeated feeding; the mosquito becomes non-infective while a few sporozoites remain in the glands, and it seems arguable that all sign of sporozoites might disappear, though most of the evidence is on infectivity. MITZMAIN (1917) showed that a specimen of *A. punctipennis* which had been infective for 14 days, during which time it had fed 8 times, was not infective on the 15th, 16th and 17th days though a few sporozoites remained in the gland when it was dissected on the 17th day. JAMES (1926) reported the depletion of sporozoites after 40 days of feeding, though some mosquitoes remained infective for 10 weeks.

Considering the common lengthy duration of infection and comments made later in this paper on the improbability of common survival for such periods in nature after the first appearance of sporozoites, it is thought justifiable in later argument to regard the proportion of mosquitoes recovering from infection in nature as negligible. Numerical allowance for its occurrence which can be made sinks into inconsequence under the influence of the improbability of prolonged survival and the probability of superposed infection.

Infectivity of Man

The infectivity of the blood donor is very variable and the evidence on it most confusing, particularly in relation to *P. falciparum*. Many factors have been said to influence it, but most attention has been paid to the density of gametocytes in the blood, the numbers of each sex, and their maturity as shown by exflagellation.

Restricting discussion for the moment to *P. falciparum*, the original statement of a lower limit of density which produced infection is by DARLING (1909, 1910) who quoted one per 500 leucocytes, said to be 12 per cmm., as the lower limit of infectivity to *A. albimanus*. His protocols do not refer to any experiments on persons with less than one to 200 leucocytes. There were 3 such patients and 2 out of 19 mosquitoes fed on them became infected, whereas roughly half the mosquitoes fed on patients with greater numbers became infected. His interest in doing the work was to determine a threshold below which persons could be discharged from hospital as being harmless to the community, and it may well be that he thought some safety margin desirable. Many subsequent workers have postulated other limits of density which produced infection. SCHÜFFNER (1919, 1938) and SCHÜFFNER *et al.* (1932) took a threshold of one gametocyte to 300 leucocytes, said to be 20 per cmm., BARBER and OLINGER (1931) took one to 100 leucocytes, MACKERRAS and ABERDEEN (1946) took 40 per cmm., and conclusions were drawn in each case depending on the differentiation of infective from non-infective people.

The experimental evidence is insufficient to support the existence of a threshold within the range of densities usually counted. KLIGLER and MER (1937) infected mosquitoes from patients with 5 gametocytes per cmm. and reported that though there might be some vague correlation between density and infectivity their results were highly irregular, and persons with 5 to 40 per cmm. infected as many mosquitoes as did those with 140 to 200 or with 340 to 1,000. In each case more than one donor and considerable numbers of mosquitoes were used. KING (1929) investigated the subject and could find no correlation. GREEN (1929) found that the lowest density of *P. falciparum* gametocytes infective to *A. maculatus* was 42 per cmm. He succeeded in infecting one out of 3 mosquitoes fed on a patient with this density and failed

to infect 54 mosquitoes fed on persons with lower numbers; JAMES (1931) did not find a lower limit of exflagellating gametocytes of *P. falciparum* infective to mosquitoes. Though he observed one (1 to 1,000 leucocytes) for *P. vivax*, he reported finding no correlation between the numbers of exflagellating *P. falciparum* gametocytes and infectivity, cases with many often being non-infective. The data presented by BOYD, STRATMAN-THOMAS and KITCHEN (1935) suggested a correlation with density of microgametocytes, but this is contradicted by original data presented by BOYD (1949, Table 84, p. 628) which could well be used to support an inverse relation but not a positive one.

There is one series of careful studies which shows an undeniable close correlation. KNOWLES and BASU (1943) maintained blood-fed *A. stephensi* in constant-temperature incubators at 50°, 60°, 70°, 80° and 90°F. Of those fed on *P. falciparum* cases a negligible proportion kept below 70°F. became infected. At 70°F. the correlation between gametocyte density in the donor and successful infection of the mosquito was close. Most of the mosquitoes were dissected before salivary infection and the data quoted below in illustration refer to gut infections only.

Donors' gametocyte count per cmm.	No. of experiments	Mosquitoes surviving to dissection	Percentage showing gut infection
0- 100 ...	3	71	0
101- 200 ...	8	270	23
201- 500 ...	9	224	59
501-1,000 ...	7	85	71
Over 1,000 ...	4	582	98

This is impressive, but a similar relation is not repeated in their 80° and 90°F. experiments, nor in similar ones by BASU (1943) using *A. annularis*. Moreover the numerous successes of other workers in infecting mosquitoes from patients with less than 100 gametocytes per cmm. cannot be ignored. It is notable that this clear positive correlation occurred at the lower threshold of temperature for *P. falciparum* development.

Reason says that there must be some range of densities within which there is a correlation with infectivity. It also suggests that the range within which this occurs might well vary according to the favourability, or unfavourability, of other factors influencing fertilization. This might account for Knowles and Basu's successful demonstration of a correlation near the lower limits of favourable temperature and in a range of densities where other evidence is so unsure, or more correctly amounts to valid evidence that correlation is not close when mosquitoes are kept at variable temperatures.

Thorough examination of a thin film as carried out in field surveys rarely amounts to examination of more than 0.01 cmm. of blood, and of a thick film of 0.1 cmm., so that the range of densities observed is almost entirely within that in which correlation is normally so hard to trace. In many cases the great majority of carriers show gametocyte counts well above the minima which have been discussed and then the argument becomes irrelevant. BASU (1947), for instance, recorded the count in 163 *P. falciparum* gametocyte carriers, only 9 of whom had less than 40 per cmm. and only 20 between 40 and 120.

The writer, on reviewing the evidence, thinks it best to ignore *P. falciparum* gametocyte counts obtained in field surveys in this connexion, and instead

to take a factor, representing the proportion of feeds on observed gametocyte carriers, regardless of density, which are infective to mosquitoes. This can then be applied to the observed gametocyte rate to convert it into the infectivity rate. The determination of such a factor seems a more direct approach to reality than the drawing of an illusory dividing line based on a critical number of gametocytes.

The situation of infectivity of *P. vivax* is much less vague. Mosquitoes can at times be infected by persons showing very low numbers of gametocytes. SWELLENGREBEL, DE BUCK and KRAAN (1937) infected one of 42 *A. maculipennis atroparvus* fed on a man with one gametocyte to 6,000 leucocytes, and 3 out of 81 on a patient with 2 gametocytes to 2,000 leucocytes. Unfortunately there was then a gap in their range of densities and the next, 1 gametocyte to 100 leucocytes, infected 47 out of 52 mosquitoes. JAMES (1931) named one exflagellating gametocyte to 1,000 leucocytes as being always non-infective. Above these very small counts there appears a regular correlation with microgametocytes in several people's work, and the use of a sliding scale seems justified where low counts are common.

Duration of the Extrinsic Cycle

The time taken for completion of sporogony to the stage of invasion of the salivary glands by sporozoites is certainly dependent on temperature, and the weight of evidence suggests that atmospheric conditions such as humidity are of little importance, though they may affect the mosquito's expectation of life and so prevent completion of the cycle. It also seems very probable that there are minimum temperatures below which development is indefinitely retarded, less than 19°C. for *P. falciparum* and below 15°C. for *P. vivax*. High temperatures are lethal to the parasite, for instance STRATMAN-THOMAS (1940) showed that exposure of anophelines, which had recently fed on blood containing *P. vivax*, to 37.5°C. for 4 hours, prevented development, while if the development had started at suitable temperatures the growing parasites were killed by 18 to 24 hours at the higher temperature. At temperatures approaching the maximum the number of successful infections of mosquitoes is decreased. Within the limits thus set the rate of development has been found by all observers to be dependent on temperature. Results have been collected by different techniques, by maintenance of the mosquitoes at steady incubator temperatures, by maintenance in rooms of reasonably constant temperature, and by recording the range of temperatures to which mosquitoes were exposed and noting the mean. The first is undoubtedly the most accurate technique, but as the last represents conditions existing in nature, it has been thought justifiable to include some reliable observations of this type in analysing the literature.

Data on the period to sporozoite development and temperature, relating to *P. falciparum* and *P. vivax* only, have been collected from WENYON (1921), JANCsó (1921), KING (1929), KLIGLER and MER (1937), STRATMAN-THOMAS (1940), KNOWLES and BASU (1943), SIDDONS (1944), BOYD (1949), and CAMBOURNAC (1942, quoted by Boyd, 1949). The times of development at various temperatures have been plotted on a graph which is presented in Figure 1. Smoothed curves have been drawn by eye to represent the mean of the observations for each of the parasites. There are considerable divergences from the smooth curve in the higher temperature ranges, but under 25°C. the findings are very homogeneous. The curves are similar to, but not identical with, those presented by Boyd for observations on *A. quadrimaculatus* infected with the two species of parasite, the chief difference being that the present curve for *P. falciparum* is steeper in its upper end, a difference which seems

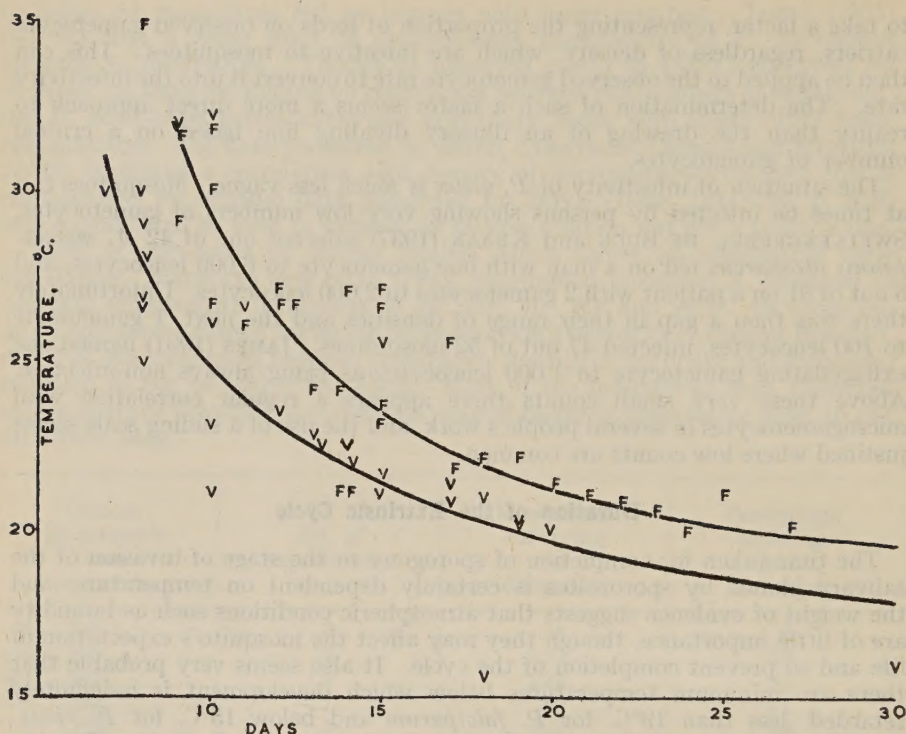


Figure 1.—The relationship of temperature to the period of extrinsic development. For sources see text. Individual records relating to *P. falciparum* are marked as F, those for *P. vivax* as V. The upper smoothed curve represents a mean for *P. falciparum*, the lower for *P. vivax*. Records of 35 days for *P. falciparum* at 20°C. and 19°C. and 38 days for *P. vivax* at 16°C. are omitted.

justified by the weight of evidence, though the importance of the change is small.

The apparent extrapolation of the curves to the right is justified by the existence of occasional data beyond the limits here presented.

Over a very large range of the equatorial region the temperature shows no great diurnal or seasonal fluctuations. In the coastal areas of equatorial Africa which are famed for their high endemicity of malaria it is remarkably constant. CLAYTON and CLAYTON (1947) give annual means of 26.9°C., 26.5°C. and 26.1°C. for Lagos, Freetown and Zanzibar; in no month does the monthly mean differ by as much as 3°C., and the assumption of typical times of extrinsic development of about 12 days for *P. falciparum* and 9 days for *P. vivax* for such places seems reasonable. In inland areas and further from the equator temperatures showed marked variations with altitude and season, but much of the central African plateau normally experiences lower temperatures. Entebbe and Kampala near Lake Victoria show very small fluctuations round 21.6°C. and 21.0°C., at which temperatures the extrinsic cycles are probably lengthened to about 20 and 15 days, and the corresponding reduction in the prospects of transmission must affect the epidemiology of disease and the requirements for its adequate control.

Frequency of Biting on Man

The frequency of biting on man as distinct from other animals is clearly a composite of the frequency of taking blood meals and the proportion of them which are on man. The amount of study on the first of these is surprisingly small. There is evidence, though not all unqualified, that in nature one blood meal is taken for each complete cycle of ovarian development by most species, the feeding and gonotrophic cycles being the same. CHRISTOPHERS (1911) first showed an appropriate method of study of the gonotrophic cycle; working on *A. subpictus* in the hot season in the Punjab he found that in the laboratory the normal interval was about 4 days, and he collected data which suggested that it was shorter, perhaps 3 days, under natural conditions. MUIRHEAD-THOMSON (1941, 1947 and 1951) used Christophers's principles of study in Assam and in West Africa and later summarized the literature. He found by his own observation that a 48-hour cycle was common in *A. minimus*, *A. gambiae*, *A. melas* and *A. funestus*, though *A. vagus* had a 24-hour cycle. Common occurrence of a 48-hour cycle is supported by other observations such as those of AFRIDI, MAJID and SHAH (1940) in the case of *A. culicifacies* in the Punjab. VISWANATHAN, RAO and RAO (1944) found that *A. fluviatilis* had a 48-hour cycle in Madras from September to November, and a 72-hour cycle later in the year. SENIOR WHITE, GHOSH and RAO (1945) studied development in the laboratory and found that in August *A. subpictus*, *A. culicifacies*, *A. vagus* and *A. fluviatilis* had a 48-hour cycle, while *A. varuna* had a longer one of about 59 hours, but in other months the cycle was longer in all species even though there was no material temperature difference. In the Sudan, LEWIS (1948) has made comparable studies and recorded data on ovarian development which indicated the possibility that the cycle in *A. gambiae* and *A. rufipes* was somewhat shorter than 48 hours.

It is probable that the time of the cycle is always dependent on temperature as well as possible specific differences, and it needs separate measurement for different seasons in different geographical regions. The evidence points to the probability that 48 hours is a very common period in the humid tropics at temperatures when malaria transmission is occurring on a material scale.

The frequency of feeding on man as distinct from other animals is studied by the precipitin test, the literature on which has been summarized by BOYD (1949, p. 661 *et seq.*). Another valuable series covering large numbers of examinations of several species is to be found in a paper by SENIOR WHITE (1947). It is clear that examinations have not yet been carried out on a sufficient scale to permit dogmatic assertions on invariable preference by any species, but they appear to fall into 3 groups: one with a marked preference for human blood, one which is more or less indiscriminate—selecting the most readily available blood meal, and one with marked preference for other species. The species which are in nature extremely important vectors of malaria do not all fall into the first group. *A. fluviatilis*, *A. funestus*, *A. gambiae*, *A. pharoensis* and *A. minimus minimus* probably fall into it, but other well-recognized carriers such as *A. culicifacies*, *A. hyrcanus* var. *sinensis*, *A. maculatus* and *A. superpictus* are clearly more appropriately placed in the second group or even the third. They may show great variations in the frequency of choosing man, and even when they do so only rarely they may transmit much malaria and maintain very high endemic malaria levels, though obviously this is only possible when they are present in considerable numbers. Such a state of affairs probably occurs with *A. culicifacies* in South India, as is evidenced by the work of RUSSELL and RAO (1942*b* and *c*).

The variations in the frequency of taking human blood far exceed those which are probable in taking blood meals as a whole and completely overwhelm

them in importance. It will be shown later that these variations have great epidemiological importance in determining the crude possibility of transmission.

Pattern of Mosquito Mortality

There are two factors in any mortality pattern, the actual death rate for any group and the variations in that death rate with age or other factor. In all animals there is some terminal age when the death rate becomes extremely high through degenerative causes, and this must undoubtedly be the case in mosquitoes. The numerous studies of the maximum length of survival of anopheline mosquitoes make it extremely unlikely that this stage of death through degeneration due to old age occurs before 2 to 3 months of survival; thus BOYD (1949) quotes the maximum period of survival recorded in the literature of a number of species, which in the majority is over 60 days and in one example of *A. punctipennis* rises to 100 days. SHUTE (1936) quotes the survival of *A. maculipennis atroparvus* to 82 days, and AFRIDI, MAJID and SHAH (1940) recovered marked *A. culicifacies* 56 days after liberation—a period which exceeded the maximum laboratory survival.

Under natural conditions the mortality must very often be such as to preclude the possibility of survival to this age of degeneration, and most workers have assumed that the hazards of wild life fall roughly equally on all age-groups, so that the death rate by ages would remain roughly equal. MARSTON BATES (1949), in a review of the literature, comments that this opinion is accepted by most workers, and HACKETT (1937) noted that it might be true in Europe.

The nearest approach to nature in studying longevity was made by RUSSELL and RAO (1942*a* and *b*). Working in Madras, they constructed a cage, 40 × 20 × 10 feet in size, which enclosed a mud hut with thatch roof, divided into two compartments and housing a calf, while in the outer part there were pools and other natural features. They liberated large numbers of freshly hatched *A. culicifacies* into this cage and at various intervals established the number of survivors by direct count. Their results are presented in figures and in normal and logarithmic graphs, and they state that the numbers decreased in geometrical progression at a common ratio of 0.5 every 2 days, which is equivalent to a daily mortality of 30 per cent. Their logarithmic graph does not completely support this, the lines being concave; 6 out of 8 veer first to the left of the common ratio line and all end on its right, which is incompatible with a true geometric progression. All the series show a greater mortality between liberation and first checking than between that check and subsequent ones, and the numbers are sufficient to make this difference statistically significant.

The process of catching every mosquito to count them in such an enclosure must have been extremely difficult. It has therefore seemed fairer to the writer to take the number counted at the first check as a base and to calculate subsequent survivors as a proportion of this figure, expecting an equal error due to failures to catch in each of the checks. Figure 2 shows a semi-logarithmic graph of the proportion of survivors in each experiment worked on this basis. The concavity is greatly diminished and together the lines give a reasonable picture of a geometric progression represented, as an average, by the interrupted line, which corresponds to a daily mortality of 22.5 per cent., which would give a 40 per cent. loss in 2 days instead of Russell and Rao's 50 per cent.

The small degree of the numerical discrepancy needed to produce this difference should be realized; it amounts to a failure to capture one mosquito out of 8. Whether this is the explanation or not, the mortality over the greater part of the life cycle is certainly nearer 22.5 than 30 per cent. per day. The inherent great value of the experiment and the light it can throw on other epidemiological factors justifies critical though appreciative examination.

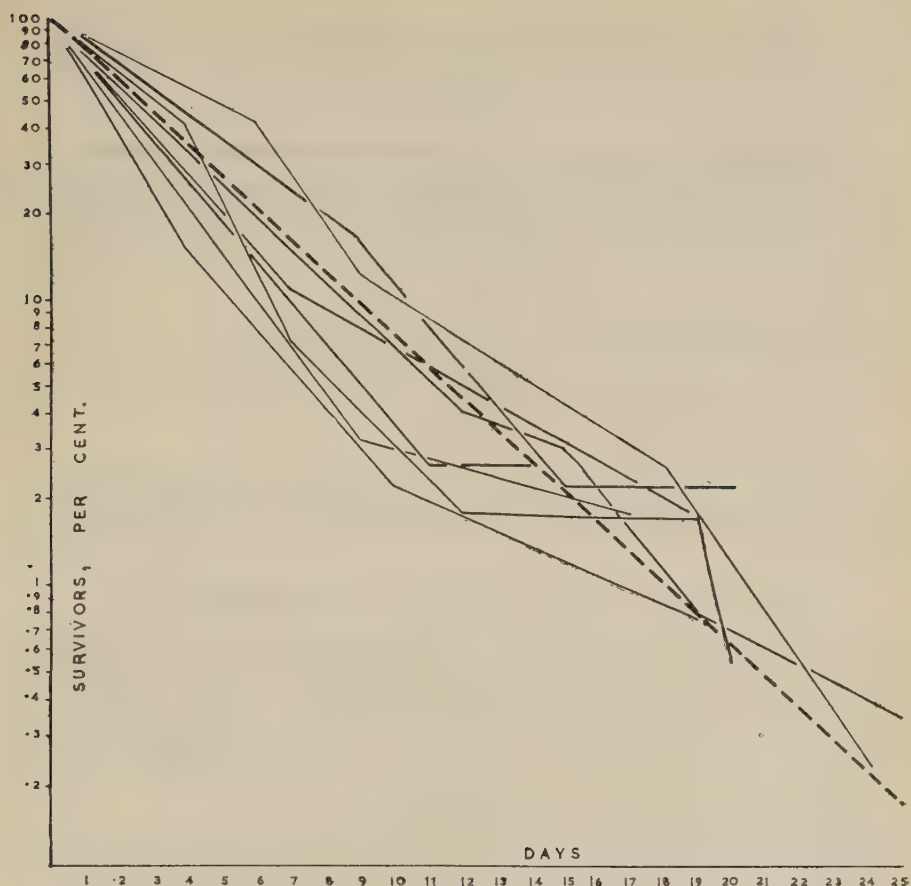


Figure 2.—A semi-logarithmic graph showing the percentage of surviving *A. culicifacies* in eight experiments carried out by RUSSELL and RAO (1942b). The number counted at the first check is taken as the origin instead of the numbers released. The heavy interrupted line represents a standard daily mortality of 22.5 per cent.

KEENER (1945) maintained *A. quadrimaculatus* under standard conditions, recording their weekly mortality, and when the data presented by him are graphed logarithmically they fall into an almost perfect straight line, showing that the mortality was in the form of a geometrical progression unaltered by age. SHUTE (1936) made careful observations on the longevity of *A. maculipennis atroparvus* with reference to oviposition. The data from the first two of his experiments, graphed logarithmically, constitute almost perfect straight lines. In the third there is a marked kink after the seventh oviposition but the numbers of survivors at this stage are very small, and when checked by the chi-square test the probability of this third experiment corresponding to the same mortality pattern remains high ($p=0.53$). The other observations which the writer has been able to trace support, in general, the contention that mortality is even throughout the ages. In particular the major series of data presented by AFRIDI, MAJID and SHAH (1940) on *A. culicifacies* is consistent with it, but in many examples in the literature there is some disturbing factor, or the data are inadequate for analysis.

Whatever the case in undisturbed nature, the assumption becomes very much more acceptable when residual insecticides are applied. In this case a hazard is introduced which is intended to outweigh all others in importance and which must fall equally on all house-haunting members of the species.

Probabilities of Mosquito Survival and the Expectation of Life

If the picture of a death rate which does not change materially with age is accepted, certain deductions follow naturally. Let p be the probability of survival through one day, the converse of the probability of dying in that time; then :—

1. The probability of surviving through n days is : p^n ;

2. The expectation of life is : $\frac{1}{-\log_e p}$ or $\frac{1}{-2.303 \log_{10} p}$

[Note : $\log_e p$ is identical with $2.303 \log_{10} p$ which, when p is a fraction, is a negative number.]

3. The expectation of life after survival through n days is : $-\frac{p^n}{\log_e p}$ and

4. These identities remain true whatever the age of the mosquito when it is first observed.

Inter-relation of the Factors to Produce the Sporozoite Rate

The expression for the sporozoite rate is most accurately derived by methods which take account of the effects of continuous change in the probability of infection, that is by methods involving the use of the calculus. This has been done by Dr. P. ARMITAGE of the Medical Research Council staff and it is hoped that he will publish his statement elsewhere. An explanation is substituted here which is more complicated in its verbal expression, and not so logically unassailable, but which makes less demand on the reader's mathematical knowledge. The symbols used are :—

- a the average number of blood meals *on man* taken by a mosquito in a day ;
- p the probability that a mosquito will survive through one day ;
- n the time in days taken for the completion of the extrinsic cycle ;
- x the proportion of bites on man which are infective to the mosquito ;
- s the proportion of mosquitoes with sporozoites in their salivary glands ;
- e the base of natural logarithms 2.71828.

Bearing in mind that a mosquito cannot have sporozoites in its salivary glands until after the completion of n days, the probability of this happening on the following day will be a reflection of the probabilities of its having taken an infective feed on the first day of its life. The probabilities for the day which follows will reflect the infective feeds on the first and second days, *less* the possibility of one infective feed being masked by a previous one. The converse of this, the probability of *not* having sporozoites on day n , $n+1$, etc., can be easily understood. By this means and by reference to the previous section it is simple to establish the three following values :—

(1) The expectation of life, already stated as :

$$\frac{1}{-\log_e p}$$

(2) The expectation of *non infected* life after survival through n days. If the average number of infective feeds taken on one day is ax , the probability of taking one or more is : $1 - e^{-ax}$, and the probability of not doing so is : e^{-ax} . The probability of surviving is p , so the probability of surviving through one day in a non-infective state is : pe^{-ax} .

The sum to infinity of the series for which this is the expression for one day is :

$$\frac{1}{ax - \log_e p}$$

But for the moment it is only desired to study the expectation of non-infective life after survival through n days, before which infectivity is impossible. To find this the previous expression must be multiplied by p^n to give :

$$\frac{p^n}{ax - \log_e p}$$

(3) The total expectation of life after survival through n days. This has already been given as :

$$\frac{p^n}{-\log_e p}$$

On consideration of the verbal definition of the above values it should be clear that the proportion of the whole life for which sporozoites will be present in the glands is expressed by :

$$\frac{(3) - (2)}{(1)}$$

$$\text{or : } s = \left\{ \frac{p^n}{-\log_e p} - \frac{p^n}{ax - \log_e p} \right\} \times -\log_e p$$

which simplifies itself to :

$$s = \frac{p^n ax}{ax - \log_e p}$$

Values of powers of p from 8 to 20 and of $-\log_e p$ for different values of p are set out in Table I. They make the working of the formula for the sporozoite rate possible without the use of logarithm tables.

It may be desired to derive values of the unknown p from given values of a , x , n and s . The nature of the expression, in which p is raised to high values, is such that this is a reasonable process, the errors of observation being minimized in the doing. Unfortunately the expression is only implicit in this respect, algebraic calculation of p being impossible, though graphic solution is simple. The known values of a , x and n are inserted and the values of s corresponding to serial values of p plotted on graph paper, the point where the graph so made intersects the known value of s gives the required value of p . This can be easily carried out for any given values, but there are so many factors involved that their mutual relations cannot be fully demonstrated over a large range of values in one graph, and a complete nomogram would be very unwieldy. A partial representation can be given on one sheet by holding one of the variables constant, and this has been attempted in Figure 3 (p. 580) which includes a number of graphs, each one of which shows the sporozoite rate for a given average daily number of infective feeds (ax) when the probability of mosquito survival has the value shown on the graph. It only refers to conditions when the extrinsic cycle lasts 12 days, a time selected for illustration as probably representative of *P. falciparum* development in the humid coastal areas of the equatorial region. Some error is introduced by applying it to warmer places where development is one or two days quicker, but very considerable error is

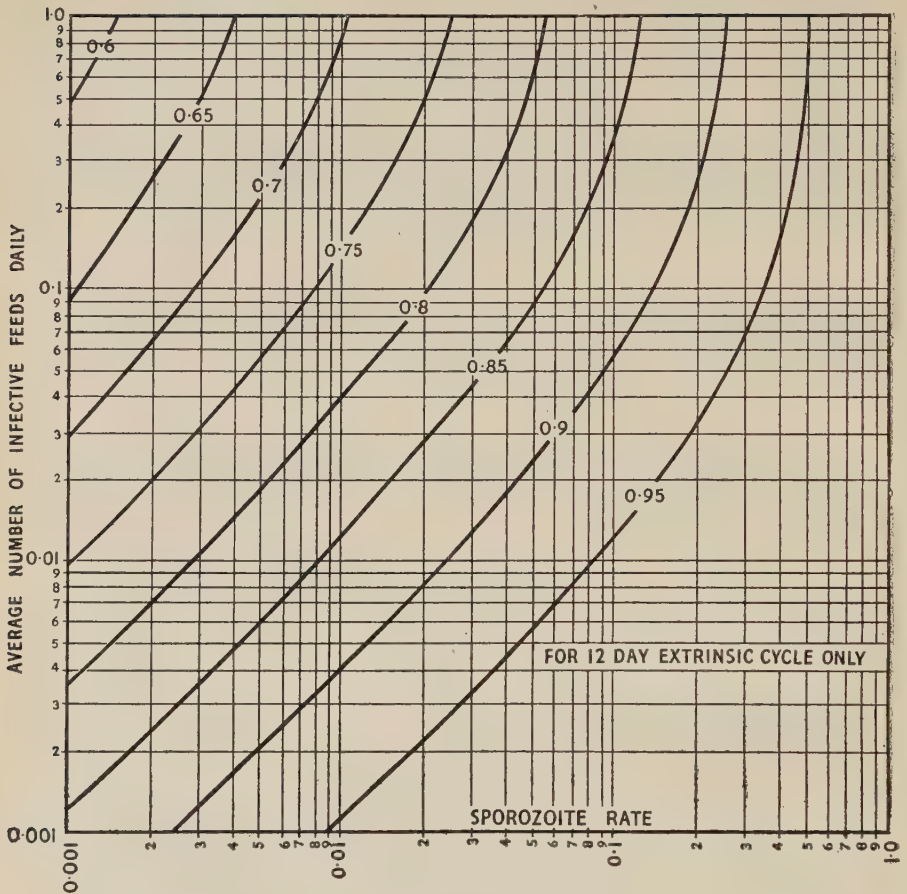


Figure 3.—A series of graphs showing the sporozoite rate corresponding to given frequencies of infective feeds. Each graph refers to a different probability of survival which is shown on the line. The frequency of infective feeds is the product of the frequency of biting man and the infective gametocyte rate.

introduced by applying it to places 5°C. cooler, where the value of n may be almost doubled. Examples in such cases should be worked separately, or general graphs to cover them, resembling Figure 2, should be prepared. This should be easy enough with the help of Table I.

The values of s , a , x and n are directly measurable but there is no practical direct method of measuring p , which is in consequence the usual unknown. The nature of the formula, in which p is raised to the n^{th} power, makes its use for this purpose entirely justifiable, errors in the estimation of the other factors being lessened in the process, and if the other factors are known within any reasonable degree of error the deduced value of p is nearly accurate. As the different graphs are very nearly parallel, interpolation between them on the radius of curvature is fully justified, and the small changes in the deduced value of p for quite material changes in given values of ax corresponding to a given value of s may be easily verified. The influence of the probability of

TABLE I
Values of p^n and $-\log_e p$

Value of p :-	0.95	0.9	0.85	0.8	0.75	0.7	0.65	0.6	0.55	0.5
p^8	0.6633	0.4304	0.2725	0.1677	0.1002	0.0577	0.0318	0.0168	0.0084	0.0039
p^9	0.6302	0.3875	0.2316	0.1342	0.0751	0.0404	0.0207	0.0101	0.0046	0.0019
p^{10}	0.5987	0.3486	0.1967	0.1075	0.0564	0.0283	0.0135	0.0060	0.0025	0.0010
p^{11}	0.5687	0.3138	0.1673	0.0859	0.0423	0.0198	0.0087	0.0036	0.0014	0.0005
p^{12}	0.5402	0.2823	0.1422	0.0687	0.0317	0.0138	0.0057	0.0022	0.0008	0.0002
p^{13}	0.5134	0.2542	0.1209	0.0550	0.0238	0.0097	0.0037	0.0013	0.0004	0.0001
p^{14}	0.4876	0.2288	0.1028	0.0440	0.0178	0.0068	0.0024	0.0008	0.0002	
p^{15}	0.4632	0.2059	0.0874	0.0352	0.0134	0.0047	0.0016	0.0005	0.0001	
p^{16}	0.4401	0.1853	0.0743	0.0281	0.0102	0.0033	0.0010	0.0003		
p^{17}	0.4181	0.1667	0.0631	0.0225	0.0075	0.0023	0.0007	0.0002		
p^{18}	0.3972	0.1501	0.0536	0.0180	0.0053	0.0016	0.0004	0.0001		
p^{19}	0.3773	0.1351	0.0456	0.0144	0.0042	0.0011	0.0003			
p^{20}	0.3585	0.1215	0.0388	0.0115	0.0032	0.0008	0.0002			
$-\log_e p$	0.0513	0.1054	0.1625	0.2232	0.2877	0.3567	0.4308	0.5108	0.5979	0.6932

Note : The fact that $-\log_e p$ is a positive number must be borne in mind.

survival in determining the sporozoite rate is so great that minor changes in it overwhelm in importance minor changes in the other factors.

Comparison with Conditions in Nature

There is no discoverable example in the literature in which all the variables concerned have been measured. The nearest approach is the series of papers by RUSSELL, MENON and RAO (1938) and RUSSELL and RAO (1940 ; 1942 a, b, c), which between them give a most detailed picture of happenings in a part of Madras. Malaria was endemic, the parasite rate of children was 32.2 per cent., the species incidence being *P. falciparum* 69.7 per cent., *P. vivax* 23.7 per cent., *P. malariae* 1.6 per cent., and mixed or undiagnosed 5 per cent. There was no significant decrease of the parasite rate up to 14 years. The disease was transmitted by *A. culicifacies* which had a sporozoite rate, on 13,145 dissections, of 0.061 per cent. The mortality of anophelines was measured as 50 per cent. every two days but it has already been suggested that 22.5 per cent. daily is a better interpretation of the data. During the period of these longevity trials the mean temperature, which was precisely recorded, exceeded 29°C. and for long it was over 30°C. so that it is fair to assume a 9-day cycle for *P. falciparum* and an 8-day cycle for *P. vivax*. These longevity tests did not cover the whole year, but the sporozoite rate for the months in which they were carried out was 0.064 per cent. The anthrophilic index based on 731 precipitin tests was 2.5 per cent., and from other data it is fair to assume a feeding cycle of 48 hours, so that the average daily number of feeds on man would be 0.0125.

All needed data exist except the gametocyte rate. If they are assembled in the form of :

$$s = \frac{p^n ax}{ax - \log_e p}$$

or :

$$0.00064 = \frac{0.775^9 \times 0.0125x}{0.0125x + 0.2549}$$

the value of 0.130 is derived for x —in other words the deduced infective gametocyte rate is 13.0 per cent. Considering that this method of working is the

opposite of that advised as a routine, this is a very good estimate of the probable figure, as errors have been greatly multiplied in the process. It is likely that the infective gametocyte rate was actually below this; the writer would have expected it, from the other parasitological data, to be about half this value, in which case the conditions would be fitted by a daily mortality of 20 per cent. rather than 22.5 per cent. The example is not quoted as one of exact confirmation but to show that the observation and the theory belong to the same universe.

Russell and Rao also estimate from direct observation that the minimum density of mosquitoes necessary to ensure the continued existence of malaria in this district lay somewhere between 8-10 and 17-20 per man-hour catching. From theory on the reproduction rate of malaria (MACDONALD, 1952) the writer would have expected 2.5 bites per inhabitant each night to be the critical level. The two figures are presented in different forms and so cannot be directly compared, but they also seem to belong to the same universe.

From these comparisons it is suggested that the theory of the sporozoite rate which is now put forward explains adequately the interrelationships between mosquito longevity, the time of the extrinsic cycle, the biting habits of the mosquito and the prevalence of infective people, and so throws light on the epidemiology of the disease. It does not throw light on the endemic level at which the parasite rate and gametocyte rate become stabilized, a subject which requires further study. It can be used particularly to measure mosquito longevity by the indirect means of measuring sporozoite rates and infective gametocyte rates, and so not only to throw light on an almost unexplored subject but also to explain some of the differences in malarial endemicity maintained by different anopheline species.

Deductions on Mosquito Longevity

The anthropophilic index of *A. culicifacies* is not always as low as that in Madras. SENIOR WHITE (1947) has recorded large series of tests in which it varied from 3.5 to 12.1 per cent., and RUSSELL and JACOB (1939) have recorded a figure of 80 per cent., which they attributed to an absence of cattle. In the place where this observation was made one infection in the glands was found in 984 dissected (0.1 per cent.), and the authors comment that *A. culicifacies* was not a strong carrier, and was only important on account of its abundance. The parasite rate was 66.4 per cent., which might indicate an infective gametocyte rate between 5 and 10 per cent. These figures could only be explained by an even higher mortality than in the area already quoted, of the order of 33 per cent. daily. It is notable from the meteorological data that this area is much drier than the other, and higher mortalities are therefore possible.

On the other hand very high sporozoite rates have been recorded. COVELL and BAILY (1932) showed rates of 1.9, 8.4, 16.3, 12.5, 14.3, 30.0, 13.1 and 6.5 per cent. in successive examinations during an epidemic in Sind, at the height of which the gametocyte rate rose to 55 per cent. in one of the schools observed. These figures cannot be equated with a mortality such as is recorded in Madras where only 10 per cent. of mosquitoes survive for 9 days. An anthropophilic index of 13 per cent. (the mean from Senior White's 2,020 records) and a daily mortality of 6 per cent. would explain them, and it seems probable that some low mortality such as this occurred because at the same time of year and in a similar climate AFRIDI, MAJID and SHAH were able to recapture *A. culicifacies* between 40 and 56 days after liberation.

Unlike the former anopheline, *A. fluviatilis* has a consistently high anthropophilic index. SENIOR WHITE (1947) records precipitin tests on specimens captured outdoors and in cattle sheds as well as houses, 44.1 per

cent. of the whole being positive for human blood, but other series show materially higher percentages. COVELL and HARBHAGWAN (1939) recorded an index of 97 per cent. in an area where the sporozoite rate was 7.6 per cent., and the parasite rate in children 27.9 per cent. The infective gametocyte rate for all ages cannot have been more than a fifth of this, and the probability of *A. fluviatilis* surviving through one day must have exceeded 0.9.

There are a number of paired observations of crude gametocyte rates and sporozoite rates for *A. gambiae*, which appears from the evidence available to have an anthropophilic index of about 80 per cent., and for which a 48-hour feeding cycle is reasonably established in the coastal parts of equatorial Africa. BARBER and OLINGER (1931) provide such data, together with information on infectivity of gametocyte carriers to mosquitoes, from which it is reasonable to state that 23 per cent. of mosquitoes feeding on them would become infected. It would appear that between 1.5 and 2.0 per cent. of bites on man in that district would be infective to the mosquito, and the observed sporozoite rate of 6.6 per cent. could only be explained on a survival probability of about 0.95, which is equivalent to a daily mortality of about 5 per cent.

WILSON (1936) collected a very valuable series in which both the gametocyte rate and sporozoite rate are recorded for 7 separate months in one locality. In analysing them the same values have been adopted for gametocyte infectivity and man-biting habit of *A. gambiae* as in the last example, and the paired data with the corresponding value of p are presented below.

Month				Sporozoite rate per cent.	Gametocyte rate per cent.	Approximate probability of survival through one day
August	12.5	6.4	0.97
October	6.3	7.1	0.95
January	5.7	12.2	0.93
March...	2.9	4.9	0.93
May	8.0	8.2	0.94
July	24.0	11.8	0.97
October	18.6	14.6	0.96

It is possible that when fresh infections were numerous the average infectivity of gametocytes was greater than at other times, and the probabilities for the first and last two months would then be over-estimated. The remarkable regularity of the series is obvious and the order of happenings is at least indicated. MCCARTHY (1941) has similar paired data for the neighbouring island of Zanzibar. His sporozoite rates refer to *A. gambiae* and *A. funestus*, for which last a lower anthropophilic index of 60 per cent. has been assumed on the basis of the available evidence. They suggest a probability of survival fluctuating between 0.91 and 0.95 for each species.

BARBER and RICE (1937) made similar observations in Egypt where malaria is carried by *A. pharoensis*, which showed an oöcyst rate of 6.7 per cent., a sporozoite rate of 0.33 per cent., an anthropophilic index of 94 per cent., and which was readily infected with malaria in the laboratory. The parasite rate averaged 22.1 per cent. in all the villages examined but with great variations which, with the inevitable possibility of error in the low sporozoite rate, make it inadvisable to be more precise than that the probability of survival cannot have been over 0.75 and may well have been materially less. The difference between the oöcyst and sporozoite rates makes a figure as low as 0.65 possible,

and the high anthropophilic index would make the maintenance of transmission possible despite such a high mortality.

This mortality might have been the result of an arid climate, but the existence of a species characteristic is suggested by the fact that BARBER and OLINGER (*loc. cit.*) found that in Nigeria this species had a sporozoite rate of 0.7 per cent. where that of *A. gambiae* was much higher. Since other factors were apparently the same this suggests a much greater mortality in *A. pharoensis* if it is anthropophilic in that country also.

An extremely interesting contrast between two species is presented by BARBER *et al.* (1936) in a survey of Cyprus. The general parasite rate was 36.6 per cent. ; 33.3 per cent. of infections were with *P. vivax*, 42.0 per cent. with *P. falciparum* and 24.5 per cent. with *P. malariae* ; 42 per cent. of the *P. falciparum* cases showed gametocytes and presumably most of the other cases also did, so that the infective gametocyte rate may well have been 10 or 15 per cent. Malaria was transmitted by *A. superpictus* and *A. elutus* [*A. sacharovi*] which showed very marked differences in their feeding habits and sporozoite rates, which are illustrated below.

	Anthropophilic index per cent.	Sporozoite rate per cent.	Estimated probability of survival through one day
<i>A. sacharovi</i>	82.6	1.8	0.8
<i>A. superpictus</i>	18.7	7.8	0.95

No precision is claimed for the estimates of longevity, but the order of the difference between the two estimates seems incontrovertible. The differences between the sporozoite rates could not be explained on any conceivable difference in susceptibility. Allowance for the difference in the parasite rates in the villages infested by the two species only tends to exaggerate the difference in estimated longevity. The great difference which has since been experienced in the ease of eradication of these two species could well be explained by such a difference in normal longevity.

Discussion

No pretence is made that the numerical value of the constants employed has been accurately calculated in the examples given, though it is thought that the conclusions on the order of anopheline mortality are broadly right. What has been attempted is to show the relative importance of these factors and how they fit together to form a sporozoite rate, which has a big influence in determining malaria incidence, and it is thought that they fit together neatly. When one of them, mosquito mortality, is deliberately changed in a control programme the values of the other factors influence the success which will be achieved in bringing transmission to an end. The determination of their proper numerical value is therefore an important part of a survey which is related to a control programme. The subjects which are of direct importance and only obtainable by local study are :—the gametocyte rate ; the proportion of gametocyte carriers infective to the local vector mosquito ; the anthropophilic index ; the anopheline feeding cycle, and the period of the extrinsic cycle in the mosquito. Their study involves additional work which may be difficult as well as novel and for which a revision of field technique would be necessary, but there is much dead wood in existing survey techniques which could be cut in partial compensation.

Summary

The factors by which the sporozoite rate is influenced are examined independently and some of the literature concerning each of them is briefly reviewed. They are:—the susceptibility of the mosquito, the infectivity of man, the duration of the extrinsic cycle, and the frequency with which the vector bites man, and the longevity of the mosquito.

It is suggested that mosquito mortality normally assumes the form of a geometric progression, the death rate remaining materially unchanged with age. On this basis formulae are given for the probability of survival through given periods, for the expectation of life, and for the expectation of life after survival through a given number of days.

These factors are brought together to show how they are related to each other in their influence on the sporozoite rate, for which a formula is presented. It is accompanied by a Table to facilitate its working in practice, and by a Figure showing in a series of graphs the relation between the frequency of infective feeds and the sporozoite rate, for varying longevities but for one duration of extrinsic cycle only.

The theory so developed is compared with a series of malarimetric data collected in South India, and it is concluded that the two belong to the same universe.

Some data from other areas are examined and approximate deductions are made on the longevity of the local vectors.

It is suggested that survey techniques need modification to include measurement of these factors which are of prime importance in the epidemiology of malaria.

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SUMMARY OF RECENT ABSTRACTS*

V. LEISHMANIASIS

VISCERAL LEISHMANIASIS

Epidemiology : Transmission

SABIDO (p. 453) records 158 cases of kala azar seen in Lisbon ; most of the patients were under 5 years of age. For treatment he advocates neostibosan given by intravenous injection daily for 12 days.

FENDALL (p. 241) reports a few cases in the central part of Kenya, which, he thinks, may be an endemic area. In one place a localized focus may have been started by soldiers who returned from service in areas where the disease is endemic. Kala azar has previously been reported from S. Arabia, but never fully confirmed ; FAWDRY and MAZHAR (p. 1096) now report two verified cases.

BHENDE *et al.* (p. 452) have previously reported an outbreak of kala azar in an institution in Bombay, which apparently originated in patients coming from endemic areas, from whom the infection was probably picked up by local sandflies. Further studies have confirmed the authors in their opinion of the origin and spread of the disease, and a reservoir of cases now exists in Bombay.

KOENIGSTEIN *et al.* (p. 533) state that the distribution of kala azar in China has changed very greatly in recent years. Formerly it was rare south of the Yangtze river, but increasing numbers of cases are now being found in Hangchow, and many dogs are infected there. The authors attribute these changes to the movements of armies and mass migration between 1937 and 1949. In Peking the incidence of human kala azar was 5.3 per 100,000 according to observations made in 1939-43 by Ho *et al.* (p. 794), but the incidence of the disease in dogs was 1.1 per cent. In villages, on the other hand, the human disease was 63 times as prevalent as in the city, but the canine disease was rarely found. The human disease, therefore, can apparently maintain itself in the absence of the canine disease.

The first recorded case of kala azar in Guatemala is described by ANTONIO CABRERA and ROMEO DE LEÓN (p. 349).

TERRY *et al.* (p. 535) describe infection of a finger with *L. donovani* in a laboratory worker who had on several occasions been bitten by infected animals.

HERTIG (p. 25) has observed in several Mediterranean countries a great reduction in the sandflies in villages in which DDT has been used as a residual insecticide for malaria control.

Precipitin tests made on *Phlebotomus* species in central Serbia indicate that all will feed on man and various animals ; none is specific in the choice of food (KOSTICH, p. 969).

LEWIS and KIRK (p. 534) have published a list of the sandflies of the Sudan. They note that an important breeding site is provided by the fissures which develop in clay soils exposed alternately to flooding and drought. Bats inhabit these fissures, and have been reported as sandfly hosts. Cracks in the walls of houses, in the northern Sudan, are usually too dry for the larvae.

Tests : Clinical Findings

CHAKRAVARTI (p. 453) has studied the plasma proteins in kala azar, showing that the albumin content progressively diminishes, and that hyperglobulinaemia

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1951, v. 48. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

is common. The low albumin-globulin ratio and the factors which influence the plasma proteins are discussed, with emphasis on liver dysfunction. In infant kala azar, UEBEL (p. 534) suggests that the disturbance of blood proteins is due to hyperglobulinaemia, with stimulation of the reticulo-endothelial system and degeneration of the liver parenchyma. There are also changes in the kidney.

CHUNG and CHANG (p. 721) report on a complement-fixation test for kala azar in which the antigen is prepared, in various ways, from infected organs of animals or man. They obtained positive results in 111 of 112 cases of kala azar, and negative in all of 83 controls.

RAGHAVAN (p. 137) has devised a method for collecting citrated blood in capillary tubes, and adding formalin to the clear plasma in the tubes for the gelification test. To facilitate reading, diffusible dyes were added. In a similar manner the Chopra test could be performed. Reconstituted serum prepared from blood dried on blotting paper is suitable for the Chopra test with 2 per cent. urea stibamine, but, in the technique used by RAGHAVAN and SATYA PRAKASH (p. 137), it was not strong enough for the aldehyde test.

In the Cutler test for adrenal sufficiency, salt is withdrawn from the diet for 52 hours, and the amount excreted in the urine during the last 4 hours is estimated. High values indicate adrenal insufficiency, and by this test CHAKRAVARTI *et al.* (p. 136) have found such insufficiency in a proportion of cases of kala azar. This insufficiency is probably the cause of the hyperpigmentation, emaciation, low blood pressure, and asthenia.

LIPPI and TRIPODI (p. 242) discuss the various types of temperature chart in kala azar, and conclude that none is characteristic.

In kala azar, agranulocytosis is relatively common in China, though rare in India. BANERJEE (p. 349), however, reports a case of severe granulopenia in a patient in India.

SEN GUPTA *et al.* (p. 454) describe an unusual form of post-kala azar dermal leishmaniasis.

BOLLIGER and MACINDOE (p. 971) report certain eye changes in a marsupial infected with kala azar.

Treatment

CHAKRAVARTI and SEN GUPTA (p. 350) show that in kala azar 90 per cent. of antimony given as methylglucamine antimoniate [Glucantime] is excreted in the urine within 48 hours, which is rather longer than in normal subjects. However, excretion is rapid, and there seems to be little chance of cumulative toxic action. SEN GUPTA (p. 25) has used this drug with success in a few cases of Indian kala azar. It has previously been used chiefly in the Mediterranean area, and GERMAIN and MARTY (p. 969) report favourably on it.

SEN GUPTA (p. 721) has used hydroxystilbamidine in kala azar in India, and reports favourably on it. The drug was given intramuscularly or intravenously, in a course of 10-15 injections, usually repeated after an interval of 10 days. It was given daily, on alternate days, or in two doses every three days.

CLAISSE *et al.* (p. 970) report a case of kala azar successfully treated with iomidine. Within a short time of completion of treatment the patient developed acute diabetes. The association of this with the treatment is discussed.

CHUNG *et al.* (p. 242) have used penicillin with success in the treatment of cancrum oris in kala azar. It has no action on the leishmaniae, but is of great value in controlling the secondary infection. Aureomycin, in various doses, was not found effective in experimental visceral leishmaniasis, by CHANG and LIU (p. 971).

DAS and SEN GUPTA (p. 350) report a case in which splenectomy failed to cure a patient who had relapsed after various treatments for kala azar. In comment Napier states that no case has yet been made out for the general adoption of splenectomy even in drug-resistant kala azar.

CUTANEOUS AND AMERICAN LEISHMANIASIS

ANSARI and MOFIDI (p. 972) describe the moist form of cutaneous leishmaniasis which they have found in troops on the Russo-Iranian frontier. The incubation period may be as short as 10 days. The authors, who many years ago had each suffered from typical oriental sore, inoculated material from these moist sores into their own legs, and reactions occurred which were regarded as characteristic of the Arthus phenomenon, indicating some degree of cross immunity.

The Montenegro test consists of the intradermal injection of a culture of leishmaniae, suitably prepared, and the local reaction is read after 48-72 hours. In Spain MERCADAL PEYRÍ (p. 722) found the test very valuable in cutaneous leishmaniasis, but noted that it was positive in some cases of tuberculous lupus.

MÉCHIN and SI HASSEN (p. 723) report favourably on the treatment of oriental sore with mepacrine infiltrations; penicillin was not effective.

ANSARI and his colleagues (p. 351) have studied the action of Glucantime against *L. tropica* both *in vitro* and in mice. They (p. 969) have used Glucantime with success in cases of oriental sore, injecting it partly into the lesions (on alternate days) and partly intramuscularly (every day). The courses comprised 12-15 injections, in one case repeated after an interval.

SALADINO (p. 351) reports a case of cutaneous leishmaniasis apparently treated successfully with aureomycin.

LOFGREN (p. 452) has studied *L. tropica* by phase and electron microscopy.

CORDERO (p. 623) reports a case of mucocutaneous leishmaniasis with extensive lesions and involvement of the rectal mucosa. SCHMIDT (p. 243) discusses the apparently favourable influence of high altitude on American cutaneous leishmaniasis and leprosy. The original paper should be consulted.

Charles Wilcocks

MALARIA

SWELLENGREBEL, N. H. **An Aspect of the Epidemiology of Malaria in Equatorial Africa.** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1951, Dec., v. 3, No. 4, 325-32. [15 refs.]

The author has made an analogy between premunition in Texas fever and in malaria in a previous paper [this *Bulletin*, 1950, v. 47, 1053]; this is repeated and the suggested harmlessness of hyperendemicity is again reviewed on a basis of findings by SCHÜFFNER in Mandailing (Indonesia) (*Geneesk. Tijds. Med. Ind.*, 1919, v. 59, 219 [see also this *Bulletin*, 1920, v. 16, 317]), by SWELLENGREBEL and VAN DER KUYP in Gansé (Dutch Guiana) [*ibid.*, 1946, v. 43, 267], GARNHAM in Kavirondo (Kenya) [*ibid.*, 1949, v. 46, 1113] and WILSON in Gombero (Tanganyika) [*ibid.*, 1937, v. 34, 141]. The first three of these are compared as follows:—

Place	Malaria incidence in children under 1 year of age	Mortality in first and second year of life
Mandailing ...	40 per cent.	42 per cent.
Gansé ...	80 per cent.	18 per cent.
Kavirondo ...	Practically all infected by nine months ...	8 per cent.

On the basis of this comparison an inverse relationship between the amount of malaria and the harm it does is postulated. The maintenance of intensive infection is said to serve two purposes :—

1. To allow the infants to raise their own active immunity under cover of a passive immunity derived from the mother ; and

2. To maintain this active immunity once it has been acquired in order to protect them when they have grown to be children and adults.

A warning is therefore given against measures that tend to lower the possibility of infection by striking at the mechanism of transmission of endemic malaria. It does not apply to moderately malarious places such as Mandailing, but does apply to areas such as Gombero, Kavirondo and Gansé. This warning ignores the advantages which the population might gain by complete control and is not accompanied by a statement of the extent by which the population would suffer from reduction of transmission. It was not accepted unconditionally at the Kampala Conference [this *Bulletin*, 1951, v. 48, 697], which recommended thorough investigations in places where there is a high degree of immunity, but there is much to be enquired into and there is reasonable hope that with the help of the World Health Organization the problem will be solved.

[The reviewer's comments are that other people reading the papers referred to may gain very different impressions from them. They might rate the severity of infection in Mandailing as greater than here stated, the lowest parasite rate collected by SCHÜFFNER in the age-group 0-1 year being 49·8, while by other reckonings or in other seasons he quotes 56·6 and 65·0. The comparable figure for Kavirondo is 175 infected out of 287 examined, or 61 per cent. positive—not materially different from the figure in Mandailing. Gansé appears much less malarious than either of these two places. At the examination now referred to by Swellengrebel the parasite rate of children (all ages) was 89 per cent., but it diminished in four months to 59 per cent., and VAN DER KUYP [this *Bulletin*, 1951, v. 48, 109] elaborates the same figures to show that the parasite rate in children under two years of age decreased from 78·3 per cent. to 30·3 per cent. The change in rates with seasons observed by both authors puts the group quite outside the description of hyperendemic malaria given by Wilson, Garnham and Swellengrebel. The present paper also ignores the fact that in Gombero, to which much reference is made, over 40 per cent. of the children died during childhood.]

G. Macdonald

JONCHÈRE, H. & PFISTER, R. Enquêtes malariologiques en Haute-Volta, Côte d'Ivoire et Guinée (Janvier-Mars 1951). [**Malaria Enquiry in Upper Volta, Ivory Coast and Guinea (January-March 1951)**] *Bull. Soc. Path. Exot.* 1951, v. 44, Nos. 11/12, 774-86, 3 figs.

Malaria conditions were investigated in three areas of French West Africa :—the southern part of Haute-Volta, the middle Ivory Coast, and a portion of

Guinea near the Liberian frontier. This part of Haute-Volta is prairie land with a rainfall of 1,100 to 1,400 mm. a year, 16 places investigated. The 6 places in the Ivory Coast visited are in a forest belt with a rainfall of 1,400 to 2,000 mm. a year. The 9 places in Guinea are, with the exception of Kankan, in forest; the annual rainfall exceeds 2,000 mm.

As many children as possible, from 0 to 14 years of age, were examined in each village. Spleen and parasite rates were determined. In some places *Anopheles* were captured, identified and dissected.

Of the 31 localities visited malaria was holoendemic in 16 (spleen index above 75 per cent.) and hyperendemic in 13 (spleen index above 50 per cent.). Endemicity was highest in Guinea. The parasite indices were in general higher than the spleen indices. The gametocyte index was highest between the ages of 6 months and 2 years, 21 per cent.: it was as low as 2 per cent. at ages 10 to 14. The general condition of these infected children was good. The species of parasites found were *Plasmodium falciparum* 93·88 per cent., *P. malariae* 7·1, and *P. vivax* 3·3 per cent. Mixed infections were found in 3·8 per cent. of children. *P. malariae* and *P. vivax* were most in evidence from 2 to 4 years of age. From 14 years of age only *P. falciparum* is found.

Of *Anopheles* captured, *A. gambiae* constituted 60·8 per cent., *A. funestus* 36, *A. rufigipes* 1·6, *A. nili* 1·15, *A. pharoensis* 0·2, *A. domicolus* 0·15 and *A. pretoriensis* 0·14 per cent. The sporozoite index of 2,958 *A. gambiae* dissected was 12·25 and of 214 *A. funestus* 6·07 per cent. The rôle of other species in the transmission of malaria is negligible.

Norman White

DE MELLO, J. P. **Survey of Malaria among the Indigenous Population in the Highlands of Kenya: with reference to Hyperendemic Areas.** *East African Med. J.* 1951, Nov., v. 28, No. 11, 465-72, 1 map & 1 graph.

"We define relapses as morbidity in chronic malarial subjects caused by renewed activity of the asexual cycle of the parasites in the human host. With recent exo-erythrocytic work, it has been suggested that no relapses but 'recrudescence' occur with *P. falciparum*. We have insisted however, upon the word 'relapses,' because the time between these attacks exceeded the time limit for the 'recrudescence.'

"During these relapses the African who is usually tolerant to malaria may fall ill with symptoms of general malaise, fever, pain in the spleen and liver area, headache and lethargy. But in July he goes down due to reinfection by the strain which by passing through the sexual cycle in the mosquito becomes virulent and which precipitates an acute attack. Children during these months die in great numbers; so also those Africans who have lost their normal splenic tissue due to constant infection of malaria. Africans found dying of malaria have had smaller spleens on the average.

"There are two vulnerable periods for malaria in the lives of the Africans:

"1. In March, April and early May.

"2. And in the months of July and August."

SCHOOF, H. F. & ASHTON, D. F. **The Decline and Last Recorded Outbreaks of Malaria in North Carolina.** *J. National Malaria Soc.* 1951, Dec., v. 10, No. 4, 306-17, 3 figs.

The incidence of malaria has been declining in North Carolina since 1937 despite the absence of intentional control measures for the early part of the period. Surveys of schools in 1937-38 showed a parasite rate of 12·2 per cent. among 1,470 children, while in 1943 re-examination of the same schools showed

one of 0.3 per cent. only among 1,216. There was some recrudescence in 1946-47, at about which time the Federal Residual Spray Programme was started and again terminated any active transmission.

The paper documents the last two known focal outbreaks of the disease as a matter of historical record. One, in Shocco Springs in 1943, was due to *Plasmodium falciparum*, the other at Chub Lake in the same year was due to *P. vivax*. Both were transmitted by *Anopheles quadrimaculatus* and ended naturally after therapeutic measures only.

G. Macdonald

BRITTO, R. S. & COTRIM, J. A propósito do índice de transmissão da malária em menores de um ano, no Guaporé. [**Infection in the First Year of Life as an Index of Malaria Transmission in Guaporé**] *Rev. Brasileira Med.* Rio de Janeiro. 1951, Sept., v. 8, No. 9, 644-50. [14 refs.]

This paper starts with a graphic account of the ravages caused by malaria during the early years of this century among workers engaged on the construction of the Madeira Mamore Railway, Guaporé, Western Brazil. Malaria remained a scourge. In 1945 Porto Velho, the chief town, with a population of 4,734, had a general death rate of 46 per thousand, approximately one-fifth of the deaths being attributed directly to malaria. The number of malaria cases reported that year was 1,390, the malaria case mortality rate being 3 per cent. In July 1946, DDT residual spraying was begun in Porto Velho and extended in subsequent years to stations all along the line. In 1950 along the line of 2,136 kilometres, 473 localities, comprising 5,831 dwellings with a population of 22,691, were treated. The total population of the region according to the census of that year was but 37,438. The improvement in health conditions is reflected in statistical returns for Porto Velho for 1950: the population had increased to 10,208. The general death rate had fallen to 18.5 per thousand; 636 cases of malaria were reported, only 2 of which terminated fatally. The marked fall in the case mortality rate of malaria may be connected with the use of chloroquine in the treatment of the disease; this drug has been used extensively since 1948.

Since 1948 use has been made of the incidence of malaria in infants under one year of age as an index of transmission. Blood films were made from infants attending welfare centres and infant clinics. These infants were divided into two groups, resident and non-resident. During the three years 1948-1950, 1,529 resident infants were examined; the percentage infection rate was 2.4. Of 367 non-resident infants examined during the same period the infection rate was 42.2 per cent. Of 343 non-resident infants born between 1947 and 1950 who were examined, 59 were below the age of 60 days; their infection rate was 20.3 per cent. Of the 284 infants from two months to one year of age the infection rate was 47.5 per cent.

Norman White

HEINZ, H. J. Neuere Untersuchungen über die Verbreitung von *Anopheles maculipennis* in Hamburg. [**Recent Investigations on the Distribution of *A. maculipennis* in Hamburg**] *Z. angew. Ent.* Berlin. 1949, v. 31, Pt. 2, 304-33, 4 figs. [31 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1952, Jan., v. 40, Pt. 1, 19.]

In view of a post-war increase in the numbers of cases of malaria in various parts of Germany, particularly Berlin, where war conditions appear to have created new Anopheline breeding places, and the occurrence of the disease in Hamburg, where war damage was also severe, a survey of likely breeding sites of *Anopheles maculipennis* Mg. in that city and its suburbs was carried out in 1947. A list of the sites investigated is given, showing the area of water in

each and an estimate of the number of larvae per sq. m. Apart from natural ponds, slow-flowing streams and parts of canals, larvae were found in bomb-craters, static water reservoirs and disused air-raid shelters. Rubbish had been tipped into some of these, and the water was discoloured, but conditions were normal for *A. maculipennis* in most of them, the water being still, sunny and clean and covered with algae. The position of each site is shown on a map, with indication of those estimated to contain 200,000 or more larvae per generation. These are considered dangerous from the point of view of transmission; they were generally rare in the densely populated areas, but were numerous in the eastern and south-eastern districts of the city and in outskirts where cattle were kept. Animal quarters containing many kinds of animals were examined for adults of *A. maculipennis*. These were commonest in pigsties, but their abundance appeared to be governed by a preference for a specific microclimate rather than for a particular type of animal. Of the collected Anophelines that oviposited in the laboratory, 61.8, 22 and 12.1 per cent. were *A. maculipennis* vars. *messeae* Flin., *atroparvus* van Thiel and *typicus*, respectively, and the rest were *A. claviger* (Mg.) (*bifurcatus*, auct.). The distribution of the varieties of *A. maculipennis* throughout the city is discussed. The summer of 1947 was hotter and drier than the average and favoured the development of the larvae. Observations of the breeding sites showed that development lasted less than 18 days, and there were probably five generations during that year.

It is concluded that there has been little change in the situation with regard to *A. maculipennis* in Hamburg since an earlier survey and little danger of a recrudescence of malaria, but that these mosquitos should be eliminated at least from the breeding places that have sprung up since the war.

BERNET, A. *Réflexions sur l'endophilie et l'anthropophilie de A. gambiae en A.O.F. [Observations on Endophily and Anthropophily in Anopheles gambiae in French West Africa]* *Méd. Trop.* Marseilles. 1951, Nov.-Dec., v. 11, No. 6, 903-10.

The author discusses the problem posed by the variability of *Anopheles gambiae* in respect of those qualities of behaviour termed endophily and anthropophily. The fact that to some extent, at some seasons, and in some districts, a proportion of the population of *A. gambiae* is distinctly exophilic and zoophilic in habit has a profound effect on the value of control methods based on insecticidal treatment of human dwellings, since there is a reservoir of *A. gambiae* ready to invade the treated places as the effectiveness of the treatment declines.

Anopheles gambiae may be better regarded not as an entirely "domestic" mosquito but as a "wild" mosquito, capable of maintaining itself on animal hosts, but feeding on human beings when they are present. With the proximity of a human community providing a good source of food, the population of *A. gambiae* is encouraged to grow beyond that which the wild hosts can maintain, and so the mosquitoes must continue to seek their food on man. They may easily do this without entering human dwellings to any great extent, depending on the habits of the local human populations. When they have fed, the mosquitoes may enter houses to rest or they may enter uninhabited buildings. The tropisms concerned in this seeking out of resting places are not different from those active in the purely "wild" *A. gambiae*. Odours of rush mats, straw, wood, and animal skins may attract them into native huts. Resting *A. gambiae* are more numerous in huts where cotton bales, firewood, etc., provide many nooks and crevices, than in the more barely furnished rooms of bungalows, and they remain longer in those dwellings where the inhabitants.

cause least disturbance. The micro-climate of the resting place may also be important, if the above factors are equal.

The author concludes that in order to combat *A. gambiae* most effectively, control measures should be extended to uninhabited buildings, and both imagocidal and larvicidal attacks should be made on the exophilic part of the mosquito population, and, in addition, research on the nature and habits of the animal hosts should be carried out.

A. J. P. Goodchild

DE OLIVEIRA, L., DE ANDRADE, R. M. & DO NASCIMENTO, R. Contribuição ao estudo hidrobiológico dos criadouros do *Anopheles tarsimaculatus* Goeldi, 1905 (= *Anopheles aquasalis* Curry, 1932) na Baixada Fluminense. [Hydrobiological Study of Breeding Places of *Anopheles aquasalis* in the "Baixada Fluminense"] Rev. Brasileira Malariologia. Rio de Janeiro. 1951, Apr., v. 3, No. 2, 151-247, 18 figs. (13 on 8 pls.) [37 refs.] English summary. [German version 248-308]

The English summary appended to the paper is as follows :—

"The authors employ the hydrobiological technique following the same processes used in scientific pisciculture; dissecting the larva of *Anopheles tarsimaculatus* seeing what was used for its food, and making a list of species which were not digested and which are the 'indicator species' of the 'Anopheline Phase' in the hydrobiological cycle of the breeding place.

"They also determine the topographic, climatic, physical, chemical, and planktonic character of breeding places.

"The phases of the hydrobiological cycle are as follows :

"1) A pluvial phase, followed soon after by a post-pluvial one, with $pH=7$ or a little less than 7, and relatively mingled with salts of calcium and magnesium, nitrates and phosphates; at this time *Sphaerella* and *Stephanosphaera* appear in the plankton.

"2) A second phase with a predominance of filamentous algae: *Ulothrix* and others. Many larvae of *Anopheles tarsimaculatus*. The pH is falling from 6.9 to around 5.

"3) The next phase has acidophilous organisms, the $pH=6$ to 4. There are numerous *Desmidiaceae*, many *Euglenaceae* and various *Closterium*: the larvae of *Anopheles tarsimaculatus* begin to diminish in number and later disappear, the medium becoming incompatible.

"4) A final phase in which the pH is very low, from 5 to 3.5, with a predominance of putrefaction algae, many *Cyanophyceae* many protozoa. This phase is incompatible with the larvae of *Anopheles tarsimaculatus*.

"5) Drying-up of the water: the cycle renews itself after further rain, or from brackish water caused by a high tide of new or full moon.

"The length of the hydrobiological cycle varies in accordance with numerous factors, one of the most important being the volume of water in the breeding place."

CORCOS, A. & CITTANOVA, A. Néphrites palustres. [Malarial Nephritis] Bull. Soc. Path. Exot. 1951, v. 44, Nos. 11/12, 736-41. [11 refs.]

Details are given of 14 patients suffering from nephritis who were treated in a hospital in Tunis during a period of 15 months. In all cases the nephritis was attributed to malaria infection, either *Plasmodium vivax* or *P. falciparum*. Considerable oedema characterized all cases. There was massive albuminuria, and macro- or microscopic haematuria with granular cylindrical casts. There was little or no urea retention; rarely any cardio-vascular involvement;

moderate hypertension ; a diminution of total blood proteins. In most cases blood cholesterol levels were below normal. Malarial nephritis is of such common occurrence in Tunisia that it is of malaria that the physician should first think when he sees a patient with nephritis, oedema, anaemia and splenomegaly.

Norman White

GUGGENHEIM, K. **Studies on the Effect of Atabrine on Vitamin A Metabolism.** *J. Nutrition.* 1952, Feb. 11, v. 46, No. 2, 141-9. [14 refs.]

" 1. Atabrine added to a diet containing 50% skim milk powder at a level of 800 mg per kilogram of ration does not impair the utilization of food by the rat, if adequate supplements of vitamin A are also given.

" 2. Prolonged treatment with atabrine has an adverse effect on the capacity of the liver to store vitamin A.

" 3. Even toxic levels of atabrine which decrease the ability of the liver to store vitamin A do not affect the requirement for the vitamin.

" 4. The absorption rate of carotene and of vitamin A is decreased by prolonged administration of atabrine."

CHAUDHURI, R. N., CHAKRAVARTY, N. K. & RAI CHAUDHURI, M. N., with a statistical analysis by S. J. POTI. **Chemotherapy and Chemoprophylaxis of Malaria. Clinical Trials in 500 Cases and Mass Prophylaxis in a Hyper-endemic Area.** *Brit. Med. J.* 1952, Mar. 15, 568-74, 1 chart.

1. *Chemotherapeutic trials.* Data regarding 500 cases of malaria treated at a hospital in Calcutta over a period of 3 or 4 years are analysed. The drugs employed and the numbers treated in each group are shown below :

Drug Used	Route of Administration	Number of cases
Proguanil (paludrine)	{ Oral	209
	{ Intravenous	12
	{ Intramuscular	12
Proguanil + pamaquin	Oral	30
Quino-pamaquin	"	13
M.5943	"	18
Chloroquine	"	75
Chloroquine + proguanil	"	13
Camoquin	"	80
Camoquin + proguanil	"	8
Neochin and 4 other indigenous drugs	"	30
Total	500

Details are given of the time of termination of pyrexia and parasitaemia and of the incidence of relapses in respect of each of the régimes adopted. The conclusion reached was that chloroquine and camoquin are the 2 outstanding drugs for the treatment of malaria, effecting in most cases clinical cure and disappearance of parasites within 2 days even with a single dose. The action of proguanil was less rapid and resistant *P. falciparum* cases were occasionally encountered. The optimum effective dose of the 3 drugs was chloroquine (base) 0.5 gm. followed by 0.25 gm. 6 hours later and 0.25 gm. on each of the second and third days : camoquin (base), 0.5 gm. (or three 0.2 gm. tablets) in a single dose ; and proguanil hydrochloride, 0.3 gm. twice daily on the first day and 0.3 gm. once daily for the next 4 days. Relapses of *P. vivax* malaria were

reduced by quino-pamaquin, which was found more effective than proguanil-pamaquin. M.5943 was found to have no advantages over the other drugs tested. Results with neochin were poor, and the other indigenous drugs tried proved useless.

2. *Chemoprophylactic trials* were carried out in 1948 and 1949 in 10 villages situated in a hyperendemic malarial tract 40 miles from Calcutta, with a total population of 1,458 persons. These were divided into 6 approximately equal groups, 5 of which received one or other anti-malarial drug, the sixth remaining untreated for comparison purposes :

Group	Number of subjects	Drug used and régime	Dose		
			Over 10 years	4 to 10 years	Below 4 years
I	235	Proguanil hydrochlor. twice weekly	0.1 gm.	0.05 gm.	0.03 gm.
II	276	Proguanil hydrochlor. once weekly	0.3 gm.	0.2 gm.	0.1 gm.
III	246	Camoquin* once weekly ...	0.2 gm.	0.1 gm.	0.05 gm.
IV	227	Chloroquine* " " ...	0.25 gm.	0.125 gm.	0.062 gm.
V	289	Quinine sulphate twice weekly	5 grains	2½ grains	2½ grains
VI	265	No drug			

*Dosage of camoquin and chloroquine is expressed in base.

The parasite rate was greatly reduced in all of the first 5 groups, the lowest figures being those relating to chloroquine and camoquin. In the proguanil groups there was some superiority of the bi-weekly over the once-weekly régime. The bi-weekly quinine group gave results intermediate between the two proguanil groups, but the differences were not statistically significant. The effect on the spleen rate is shown below :—

Group	May 1948	February 1949	October 1949	February 1950
	Spleen rate per cent.			
I	55.4	24.4	33.0	26.8
II	72.8	35.6	33.5	26.0
III	64.2	16.4	26.3	12.4
IV	57.7	18.2	25.7	8.8
V	—	—	53.4	43.1
VI	61.2	50.6	54.2	55.4

The recorded incidence of malaria in the various groups (parasite positive cases only) was 21.54 per cent. with bi-weekly proguanil, 12.28 per cent. with weekly proguanil, 3.12 per cent. with camoquin, 2.27 per cent. with chloroquine and 26.1 per cent. with quinine ; as compared with 62.98 per cent. in the comparison group. It is noted, however, that these figures cannot be regarded as strictly accurate.

The conclusion reached was that both chloroquine (base, 0.25 gm. weekly) and camoquin (base, 0.2 gm. weekly) afford a high degree of protection from malaria and effect a marked reduction in splenomegaly, and that they are superior to proguanil (salt, 0.3 gm. weekly or 0.1 gm. bi-weekly) in both respects.

It is considered that where anti-mosquito measures are impracticable chemoprophylaxis should take an important place in the suppression of malarial fever.

G. Covell

RUIZ-SANCHEZ, F., CASILLAS, Josefina, PAREDES E., M., VELAZQUEZ, J. & RIEBELING, Rebeca. **Terramycin in the Treatment of Malaria.** *Antibiotics & Chemotherapy*. New York. 1952, Jan., v. 2, No. 1, 51-7, 10 figs.

Two patients suffering from malaria (one *P. vivax*, one *P. falciparum*) were treated with terramycin with results described as "encouraging" [this *Bulletin*, 1952, v. 49, 12]. The authors now record the treatment of 15 more cases (12 *P. vivax*, 3 *P. falciparum*) with the same drug. Most of the clinical studies were carried out at Sauta, a small hamlet on the Pacific coast of Mexico, and the remainder at Guadalajara, a city of 400,000 inhabitants situated 4,950 feet above sea level, where malaria incidence is low. The ages of the subjects treated ranged from 15 months to 50 years. In 94 per cent. of the cases the spleen was enlarged, and in two instances it projected to the umbilical region. In 4 of the cases therapy was started on the first or second day of fever, while in the remainder the patients were allowed to have several paroxysms before treatment was commenced. Terramycin was given orally in 250 mgm. capsules, the daily dosage varying from 222 mgm. to 35 mgm. per kgm. body weight. The total daily dose was administered in 4 equal portions at 6-hour intervals for periods of 4 to 10 days.

Febrile paroxysms persisted for one to 5 days after the commencement of therapy. In *P. vivax* cases parasites disappeared from the peripheral blood in 3 to 9 days (average 6.7). In *P. falciparum* cases, asexual parasites disappeared in 4 to 5 days, the gametocytes remaining apparently unaffected.

[Lack of uniformity as regards premunity and age of the subjects treated, time of the disease at which treatment was started, duration of treatment and dosage employed, make it difficult to draw valid conclusions from the small series of cases studied. To the reviewer it appears unlikely that terramycin will prove of practical value as a therapeutic agent for malaria.] G. Covell

RULE, W. **Chloroquine as a Malarial Prophylactic in Indigenous Children of Central Africa.** *Ann. Soc. Belge de Méd. Trop.* 1951, Dec. 31, v. 31, No. 6, 683-92, 1 fig.

This study was carried out during 1948 at a mission post in the Belgian Congo, near the head waters of the Congo River, the object being to assess the effect of weekly doses of chloroquine in suppressing clinical malaria and to determine the optimum dosage of the drug for small children. The subjects treated were 30 children of indigenous inhabitants, all with a history of frequent malarial attacks. There had been no fewer than 174 cases treated for clinical malaria among the members of the group during the previous 12 months. Twenty of the 30 children had had repeated thick blood smear examinations at the hospital without a single negative finding. Their economic status was extremely poor. The region is described as highly endemic for *P. falciparum* malaria, over 90 per cent. of the parasites seen being small ring forms of this species.

The preparation used was Aralen (chloroquine diphosphate), each tablet containing 0.25 gm. of the salt, or 0.15 gm. of the base. The dosage given was :

Weight less than 10 kgm. (22 lb.) : 0.0625 gm. chloroquine diphosphate ($\frac{1}{4}$ tablet).

Weight 10 to 15 kgm. (22-33 lb.) : 0.125 gm. chloroquine diphosphate ($\frac{1}{2}$ tablet).

Weight 15 to 30 kgm. (33-66 lb.) : 0.25 gm. chloroquine diphosphate (1 tablet).

Weight 30 to 50 kgm. (66-110 lb.) : 0.375 gm. chloroquine diphosphate ($1\frac{1}{2}$ tablets).

On the first day each child received double his prescribed dose and on each of the 2 succeeding days a single dose. Thereafter each was given a single dose weekly. There was no evidence of intolerance to the drug. For a variety of reasons it was not possible to administer the drug to all the children over the whole year. The longest treatment was for 55 weeks and 17 were treated for 6 months and over.

The weekly dose was given each Monday and a thick blood smear was made every Saturday. Out of 847 smears examined, 23 (2.7 per cent.) were found to contain *P. falciparum*. In only 5 of these cases was there a concomitant febrile response ; on the other hand, there were 13 instances of pyrexia without demonstrable parasitaemia, which responded readily to anti-malarial drugs and were considered in most instances to be malarial in nature.

The author concludes that chloroquine is highly effective in suppressing clinical malaria and in reducing parasitaemia. He notes, however, that the suppressive action of the drug appeared to be somewhat less effective during the latter half of the experiment, and that small children 2 years old or less required a relatively higher dose than older ones to protect them from fever and parasitaemia. He suggests that the optimum dosage for suppression is probably somewhat higher than the scale adopted during the study here recorded.

G. Covell

MERLE, F. Paludrine et prophylaxie scolaire et pré-natale du paludisme.

[**Proguanil as a Malaria Prophylactic among Schoolchildren and Pregnant Women**] *Méd. Trop.* Marseilles. 1951, July-Aug., v. 11, No. 4, 613-21.

The observations recorded were carried out in Brazzaville. In one school 66 African children from 6 to 9 years of age were each given 0.05 gm. ($\frac{1}{2}$ tablet) of paludrine [proguanil] three times a week over a period of 6 months. In a second school 53 children received the same dose four times a week for 7 weeks. Though there was some unavoidable irregularity in the administration of the drug the parasite indices of the children were reduced by more than a half, and the enlargement of spleens disappeared very rapidly in the majority of cases, sometimes in a spectacular manner. In Brazzaville *Plasmodium falciparum* is the predominant parasite.

In Brazzaville, malaria has been responsible for a very large number of abortions, premature births and still-births. After a preliminary trial on 20 pregnant women infected with malaria, the results of which are recorded in detail, 250 African women were treated and 100 other untreated similar patients were kept under observation as a control. Each treated woman was given 0.30 gm. of paludrine once a week. The treatment was given during the last 3 months of pregnancy in all cases, in some cases for 6 months. Of 100 treated women in one group specially studied all but one gave birth to live infants at full term : the one patient who was delivered of a dead child was in the bush at a distance from Brazzaville when labour started. Among the 100 untreated

women observed as a control there were 5 abortions and 6 still-births. There was no evidence of syphilis in either group of patients. In the treated group 10 women had marked visceral signs of malaria. No parasites were found in the blood of any of the new-born infants.

If such anti-malarial treatment were given regularly to all pregnant African women in Brazzaville, from 250 to 300 more infants would be born alive in that city each year than at present.

Norman White

WILSON, T., MUNRO, D. S. & RICHARD, D. R. **Proguanil-Resistance in Malayan Strains of *Plasmodium vivax*.** *Brit. Med. J.* 1952, Mar. 15, 564-8, 4 figs. [15 refs.]

During the past 5 years, proguanil has been used with conspicuous success throughout the Federation of Malaya for the prevention of malaria. It was first adopted for routine prophylaxis by the Army in Malaya in place of suppressive mepacrine in 1949, with no apparent effect on the malaria sickness rate. In the latter months of 1950, however, an outbreak of malaria occurred in a British Army unit operating in the Tampin District of Negri Sembilan, and this led to the institution of the enquiry now reported. The total strength of the unit was 600 men, of whom 350 might be engaged in jungle operations at any particular time. The official protective dose was 100 mgm. proguanil daily. Four cases of malaria occurred between the return of the unit from Singapore in mid-April and the end of July 1950. Data regarding subsequent primary attacks of malaria in the unit up to April 9, 1951, are given below :

Species of parasite	1950					1951				Total
	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr. (1-9)	
<i>P. falciparum</i> ...	2	1	3	9	9	4	1	3	3	35
<i>P. vivax</i> ...	4	2	1	7	7	2	3	3	0	29
Total ...	6	3	4	16	16	6	4	6	3	64

The abrupt increase in November and December 1950 and most of the cases occurring thereafter came from 2 detachments which had recently started night patrols along a particular section of the main railway line. From July 1 1950 to April 9 1951 there were 67 attacks of primary malaria among the 600 men of the Tampin unit, whereas only 34 cases occurred during the same period out of several thousand men operating elsewhere in Malaya. It was evident that either anti-malaria discipline was poor in that area, or else that the local malaria parasites possessed some unusual feature.

EDESON and FIELD [this *Bulletin*, 1950, v. 47, 437] had previously reported the presence of *P. falciparum* malaria resistant to treatment with proguanil in this area, haphazard drug administration being regarded as the most likely cause. At the time of their report strains of *P. vivax* resistant to proguanil had not yet been encountered. In view of the increased incidence of *P. vivax* malaria now apparent it was arranged that infections with this species of parasite should in future be treated with proguanil, so as to obtain information as to the response of erythrocytic forms to the action of the drug. The next 3 patients with acute *P. vivax* malaria from the Tampin unit were accordingly given 300 mgm. proguanil daily for 7 days, after which they reverted to the standard

protective dose of 100 mgm. per day. Clinical response was satisfactory, but all 3 patients were readmitted to hospital with febrile and parasitological relapses 11, 16 and 17 days respectively after their discharge. None of them had been out on operations since their discharge from hospital and each man affirmed that the daily dose had been taken with unfailing regularity. A more strictly supervised investigation was now put into force, but only 3 more cases of *P. vivax* malaria became available for study before the unit left Malaya. The history of these 3 cases was similar to that of those previously investigated, overt attacks occurring 7, 12 and 13 days respectively after discharge from hospital, in spite of a daily dose of 100 mgm. proguanil.

Between June and September 1951 41 cases of malaria (22 *P. falciparum*, 19 *P. vivax*) occurred among the unit which took over the Tampin camp and operational areas in April of that year, but it was possible to study only one *P. vivax* case in hospital. The patient had been in Malaya for 10 months and in the Tampin District for $2\frac{1}{2}$ months. There was no previous history of a malaria attack. Proguanil prophylaxis was said to have been regular and the drug was present in the urine when the patient was admitted to hospital. This infection proved more obviously resistant to proguanil than any of those previously observed. Treatment with 300 mgm. of the drug daily for 10 days effected rather slow parasite clearance in the primary attack. Parasitaemia reappeared after 9 days on a suppressive dose of 100 mgm. daily, followed 3 days later by an overt febrile attack. Parasites persisted throughout a further course of 400 mgm. daily for 10 days; the attack was then terminated with quinine.

The possible explanations for the findings summarized above are subjected to critical discussion. Irregular dosage could not be excluded as a possible factor in the excessive incidence of malaria among the troops operating in the Tampin District, but the authors are inclined to favour the view that the *P. vivax* patients treated with proguanil were infected with a strain of parasite whose erythrocytic forms were already partially resistant. They stress the urgent need for controlled experiments to determine whether or not resistance to erythrocytic forms implies that pre-erythrocytic stages of the same strain of parasite may complete their development and thus render possible the subsequent occurrence of overt malarial attacks despite regular prophylactic dosage with proguanil from the date of infection.

G. Covell

EGYPT, GOVERNMENT OF: Ministry of Public Health: Medical Section (Gambiae Eradication Service). **Report on *Anopheles gambiae* in Egypt 1942-1945** 166 pp. of text, numerous graphs & half-tone photographs. [In Arabic.] 1950. Cairo: Government Press. Also separately issued mimeographed English translation of text and main tables.

In 1942 severe outbreaks of malaria occurred in Egypt along the valley of the Nile from the Sudanese frontier to Assiut. They were found to be associated with the presence of *Anopheles gambiae* which had not previously been recognized in Egypt. Severe epidemics occurred in 1943 and 1944. During this period a scheme of eradication of *A. gambiae* was started based on the principles previously used in the eradication of that species from Brazil. Success seemed to have been achieved in the early part of 1945 and in consequence larval control measures were abandoned, and the search for adults and larvae was intensified. Throughout what would have been the epidemic season and despite very energetic work no *A. gambiae* were discovered.

Although this epidemic and the policies which followed it were of great moment in the world of public health, they were not much noted at the time,

being over-shadowed by other happenings. An account was given by SHOUSHA [this *Bulletin*, 1949, v. 46, 438]. It was a lucid description of the principal happenings, which, however, did not go into those details of technique which might be useful to workers in other campaigns. The present mimeographed work gives essentially the same account as that given by Shousha but in much more detailed form, complete with full statements of the nature of the work of each type of employee in the system, details of equipment and methods of checking. Without adding much to the colloquial account of the epidemic it adds greatly to the type of detailed information which would be welcomed by the person engaged on a comparable scheme and anxious to learn from the experience of Egypt.

G. Macdonald

EJERCITO, A. **Agricultural Control of Malaria.** *J. Philippine Med. Ass.* 1951, Oct., v. 27, No. 10, 591-607, 6 figs. & 8 pls. [12 refs.]

Malaria is carried in the Philippines by *Anopheles minimus flavirostris* and has in some areas been incidentally controlled by agricultural measures intended to improve rice land, and the deliberate extension of combined works of this type is to be encouraged on an experimental estate and a dairy farm on which there are 292 hectares (721 acres) of potential rice land. Plans have been made for terracing and filling of streamlets by the use of tractors.

The area actually completed is small, and the estimates of probable costs and improvement in land value resulting have therefore an unrealistic air.

The author has high hopes for his scheme and gives numerous sketch plans and photographs in which the nature of the work can be studied.

G. Macdonald

DOWNES, W. G. & BORDAS, E. *Anopheles aztecus*, **Malaria, and Malaria Control in the Valley of Mexico.** *J. National Malaria Soc.* 1951, Dec., v. 10, No. 4, 350-58. [17 refs.]

The Xochimilco region of the Valley of Mexico is 7,426 feet above sea level, and has mean summer and winter temperatures of 61°F. and 48°F., with not infrequent frosts in the winter. The rainfall varies from 1,360 to 2,364 mm. (54 to 93 inches) and falls mainly between May and October. Malaria, due to *Plasmodium vivax*, is endemic with an annual peak of incidence in the late autumn, and 5 measures of the parasite rate in 1947-48 showed values varying from 8.6 to 1.1 per cent. Only two possible anopheline vectors are present, *Anopheles aztecus* and *A. pseudopunctipennis*, but the latter is in such small numbers that it could not be responsible for the endemicity. Natural oöcyst and sporozoite infections of *A. aztecus* have been found by Downes and Bordas [this *Bulletin*, 1950, v. 47, 587] while it has been shown by SANDOVAL *et al.* (*Rev. Inst. Salubridad. y Enferm. Trop.*, 1950, v. 11, 149) that this species is moderately susceptible to laboratory infections. The present authors give a brief review of its biology.

Control was attempted by the application of DDT (200 mgm./sq. ft., 50 per cent. water wettable powder), and BHC (20 mgm. gamma isomer/sq. ft., Gammexane P. 520) to houses and other shelters throughout the town of Mixquic in 1948, and in houses near water in 1949. Entomological and parasitological surveys showed that success was complete. It is believed that one application of DDT every 2 years will be enough to maintain control.

G. Macdonald

- i. VARGUES, R. Étude sérologique de l'infection expérimentale du rat blanc par *Plasmodium berghei* : disparition de l'alexine. Présence d'anticorps fixant le complément. [**Serological Study of Experimental *P. berghei* Infection in White Rats. Disappearance of Complement. Presence of Complement-Fixing Antibodies**] *C.R. Soc. Biol.* 1951, Aug., v. 145, Nos. 15/16, 1134-6.
- ii. —, FABIANI, G. & FULCHIRON, G. Étude sérologique de l'infection expérimentale du rat blanc par *Plasmodium berghei*. Variations quantitatives de la sensibilisatrice et de l'alexine au cours de la maladie. [**Quantitative Variation in Antibody and Complement during the Disease**] *C.R. Soc. Biol.* 1951, Sept., v. 145, Nos. 17/18, 1298-300.

i. This paper described the methods used for testing the presence of humoral antibodies and the drop in complement in the serum of rats before and after the crisis of *Plasmodium berghei* malaria. The antigen is prepared as follows : the liver of a rat dying of the disease is kept in the refrigerator for 4 or 5 days, and is then ground up with 0.9 gm. of sodium chloride ; 4 hours later, 100 cc. distilled water are added and the suspension is kept in the refrigerator for several days, after which it is centrifuged for 2 hours at 3,000 revolutions. The supernatant fluid is the antigen, and the reaction is performed with the Kolmer technique.

ii. Serological studies in human or simian malaria have been hindered by the difficulty of obtaining sufficient material to act as antigen ; in infections with *Plasmodium berghei* a plentiful supply is available in watery suspensions of heavily parasitized liver [see above]. The amount of complement and of antibodies as shown by fixation of complement in the cold (Kolmer technique) was determined on groups of white rats in various stages of infection with *P. berghei*. Complement steadily fell as parasitaemia rose, and in the second week of infection disappeared, only to reappear—first to a figure above normal—after spontaneous cure. Antibodies were first demonstrated about the 8th to 10th day of parasitaemia—at a dilution of the serum of 1/4 which rose to 1/20 by the 15th day. The titre stayed at this figure for 2 months ; even at 6 months it was still 1/5 in one animal. The authors in a rather unconvincing table attempt to show the relationship between the density of parasites and the titre of the serum.

P. C. C. Garnham

BALDI, A. & DELLA ROCCA, L. Sulla terapia dell'infezione da "*Plasmodium berghei*" nel topo. [**Treatment of *Plasmodium berghei* Infection in Rats**] *Riv. di Malariologia.* 1951, Aug., v. 30, No. 4, 173-93. [10 refs.] English summary (6 lines).

The experiments described were designed to test the relative efficiency of 8 anti-malarial drugs in the control and eradication of *Plasmodium berghei* infection in rats. Eight rats were used for testing each drug. All the rats were infected together by the subcutaneous injection of blood taken from an animal with a very heavy infection, not less than 20 per cent. red cells infected. The infecting blood was mixed with an equal part of a 3 per cent. sodium citrate solution ; each experimental animal was given 0.05 cc. Untreated, such rats invariably die within 13-15 days.

In each case the drug under test was given daily for 5 days, from the 5th to the 9th day in 4 rats, the day of infection being reckoned as the 1st day, and from the 8th to the 12th day in the other four. The drugs were given by

mouth : the daily dose was suspended in a small quantity of sweetened condensed milk diluted with an equal quantity of water. In this form the drugs were readily taken by the rats except for those animals that were almost moribund. The doses of the drugs given were from one and a half times to twice the usual human dose on a body-weight basis : the relative body-weights were taken as 1 : 3,000. The results of the experiments may be summarized as follows : the daily dose of each drug given to rats is noted. Quinine (1 mgm.) inadequate as a suppressive and failed to eradicate infection ; atebirin [mepacrine] (0.5 mgm.) good suppressive but very limited value for eradication ; plasmoquine (0.01 mgm.) inadequate suppression and no eradication value ; paludrine [proguanil] (0.5 mgm.) only moderate suppressive value and failed to eradicate infection ; chloroquine (0.5 mgm.) very effective in suppression and eradication of infection ; none of the rats treated with this drug suffered any relapse during the 60 days they were under observation ; camoquin (0.5 mgm.) nearly as effective as chloroquine but 2 rats relapsed ; pentaquine (0.05 mgm.) moderate suppressive value but of little value in the eradication of infection ; a sulphone [*Sulfone*] (5 mgm.) fairly successful in controlling and eradicating infection.

Norman White

KRUSZYŃSKI, J. **A Microchemical Study of *Plasmodium gallinaceum* by Micro-incineration.** *Ann. Trop. Med. & Parasit.* 1951, Sept., v. 45, No. 2, 85-91, 3 text figs. & 11 figs. on 2 pls. [51 refs.]

Using *Plasmodium gallinaceum* in an infection affecting over 90 per cent. of the erythrocytes, the author carried out an investigation on the distribution of the mineral components in the parasites and the host-cells. For this purpose the micro-incineration method was employed, and the results were assessed by examination of the blood films (spodograms) with the phase-contrast microscope and their comparison with stained control preparations, which were examined in transmitted light, in dark-field illumination and in incident light. For the analysis of the chemical constituents the following methods were used : the sodium cobaltinitrite test and formation of K/Na crystals for K ; formation of CaSO_4 crystals for Ca ; examination in incident light and HCl ferro- and ferricyanide tests for Fe.

It was found that the ash of chick blood cells (erythrocytes and leucocytes) and of the parasites themselves, when viewed under the phase-contrast microscope, had a similar appearance to these elements seen in stained preparations. The micro-chemical tests indicated that the mineral residue in the parasites increased with their maturation, and the amount of K, Na, Ca and P salts is greater in the ash of infected erythrocytes than in normal ones. It is thought that this increase may be correlated with an augmented metabolism. It is well known that the malaria parasites consume haemoglobin from the host-cells, which are gradually decolorized. Since the ash from the uninfected area of parasitized red cells had the same appearance, density and opacity as in normal cells, it is evident that the parasite utilizes only the part of the erythrocytic stroma which is adjacent to it. Hence it is concluded that the extra quantities of K, Na, Ca and P are absorbed from the blood plasma through the erythrocyte membrane. As regards the nucleus of the parasite, its ash contains a heat-resistant and water-insoluble component, which might correspond to phosphorus, perhaps linked to nucleic acid. Microincineration tests also confirmed the presence of iron in malarial pigment.

The appearance of the specimens in spodograms are illustrated in a number of figures.

C. A. Hoare

MUNIZ, J., SOARES, R. & BATISTA, S. **On a New Species of Plasmodium parasite of the *Ramphastos toco* Müller, 1776.** *Plasmodium huffi* n. sp. *Rev. Brasileira Malariologia*. Rio de Janeiro. 1951, Apr., v. 3, No. 2, 345-62, 79 figs. (55 coloured) on 6 pls. [14 refs.] [Portuguese version 339-44]

A malaria parasite was discovered in the blood of a toucan (*Ramphastos toco*) from the State of Goiaz, Brazil, and is named *Plasmodium huffi*. The parasite is of the large type with elongated gametocytes. Multiple invasion of corpuscles is common, a vacuole may persist even in the schizont stage, and the number of merozoites varies from 6 to 8 in acute to 20 to 30 or more in chronic infections. The asexual cycle occupies 48 hours. The exo-erythrocytic cycle is said to be of the mexicanum type [see this *Bulletin*, 1944, v. 41, 827] with parasites occurring in thrombocytes (92 per cent. [? 72 per cent.]) lymphocytes (20 per cent.) and monocytes (8 per cent.) in the peripheral blood, and in macrophages and primitive red and white blood cells in the organs (bone-marrow, spleen, liver, lung, but not brain). The number of merozoites in the exo-erythrocytic parasite varies from 4 to more than 100 according to the size of host cell invaded, and the merozoites are apparently round and not elongated. Natural infections were of moderate intensity (up to 22 per cent. of erythrocytes infected); artificial infections were of greater density and always ended fatally. Inoculations into canaries, turkeys, ducks, pigeons and chicks failed to take.

[Although illustrated by 6 coloured and uncoloured plates, this paper is unfortunately accompanied by few details. The artificial infections are not described (the type of bird used is not even mentioned), and it is impossible therefore to be convinced that the elongate gametocyte did not belong to a *Haemoproteus*; it is not stated if the exo-erythrocytic parasites were found in smears or sections, and the type of "macrophage" cell is not noted. In these circumstances, one remains uncertain whether the latter type of development really occurred in cells of the fixed reticulo-endothelial system, in addition to wandering cells—that is, whether the parasite really belongs to the mexicanum rather than to the elongatum type.]

P. C. C. Garnham

TRYPANOSOMIASIS

MONNET, A. & BAYLET, R. Contribution à l'étude des constituants biologiques du sang chez les malades trypanosomés: la cholestérinémie chez le trypanosomé. [Study of Biological Elements in the Blood in Trypanosomiasis: Evidence of Cholesterol Levels] *Bull. Soc. Path. Exot.* 1951, v. 44, Nos. 11/12, 786-93, 2 graphs.

Serum cholesterol has been determined in normal Africans and in patients with trypanosomiasis. The mean value in 100 cases for the normal serum cholesterol of Sudanese was 1.26 gm. per litre (limits 0.90-1.60 gm.), a figure considerably lower than European values. In the sufferers from trypanosomiasis the serum-cholesterol values were markedly diminished in untreated or new patients. This decline in serum-cholesterol was particularly marked in the first stage of the disease, slightly less in the second stage. In those already treated or former patients the values had returned to normal, and in the second stage even slightly exceeded it.

J. H. Birkinshaw

MONNET, A. & BAYLET, R. Contribution à l'étude du métabolisme du mélaminyl 4 phényl-arsénodithioglycérine en solution dans le propylène glycol : son passage dans le liquide céphalo-rachidien. [**Penetration of Mel B into the Cerebrospinal Fluid**] *Bull. Soc. Path. Exot.* 1951, v. 44, Nos. 11/12, 754-8.

Having studied blood levels and the urinary excretion of Mel B after intravenous injection [this *Bulletin*, 1951, v. 48, 531; *ibid.*, 958], the authors turned to an investigation of the drug's power of penetrating into the cerebrospinal fluid. Details are given of the methods of estimation used.

The observations were made in people who were in fairly good condition though infected with sleeping sickness (presumably in the lymphatico-blood stage of infection). The standard intravenous dose of 3.6 mgm./kgm. was given daily, and estimations of unchanged Mel B or of arsenic, or both, were made in 11 patients after a single injection, in 3 patients after 2 injections, in 12 patients after 3 injections, and in 5 patients after 4 injections.

Conclusions reached were that it is sometimes possible to detect arsenic as well as unchanged Mel B in the cerebrospinal fluid within 24 hours of the third or fourth injection, but not after the first or second injection. The fourth dose did not seem to increase the chances of penetration into the fluid. The amounts detected were very small, the maximum arsenic content being only 0.15 mgm. per litre, and on only one occasion was more than a trace of unchanged Mel B found.

E. M. Lourie

MONNET, A. & BAYLET, R. Étude de l'élimination urinaire du 3854 R.P. (Mel-B Friedheim-Arsobal Spécia). [**Urinary Excretion of Mel B**] *Méd. Trop.* Marseilles. 1951, Nov.-Dec., v. 11, No. 6, 893-902.

See this *Bulletin*, 1951, v. 48, 958 for an earlier summary of this paper in mimeographed form.

UNTI, O. & DA SILVA, T. L. Moléstia de Chagas no vale do Paraíba, Estado de São Paulo. Nota sobre profilaxia e epidemiologia. [**Chagas's Disease in the Paraíba Valley, São Paulo. Notes on its Epidemiology and Prophylaxis**] *Arquivos de Hig. e Saúde Pública.* S. Paulo. 1951, Sept., v. 16, No. 49, 131-8, 3 figs. English summary.

In two districts of Paraíba Valley, Queluz and Areias, until recently neither cases of Chagas's disease nor the vectors of *T. cruzi* had been met with. The authors, however, undertook the investigation anew and in Areias, both its urban and rural parts, found specimens of *Triatoma infestans*. Samples of blood were taken from 17 persons for the Machado-Guerreiro reaction; none proved positive. In Queluz County, however, the infection was common. In 25 huts 1,697 specimens of *Triatoma infestans* were captured, 1,579 in the urban and 118 in the rural areas. Of the huts in the County 5.7 per cent. were found infested and 20.35 per cent. of the bugs examined were infected. One hundred and thirty-six samples of blood were taken, unselected as regards sex or age [so details of sex and age are omitted]; 11 (8.09 per cent.) were positive by the Machado-Guerreiro test, 14 (10.2 per cent.) were doubtful and the remainder negative. Spraying the huts with BHC, 10 per cent. gamma isomer, has been, it is said, very effectual; this is to be the subject of a later report. Incidentally, it is mentioned that in the Rezende municipality, a place in the same Valley of Paraíba, 3 kilometres from Queluz, but in the State of Rio de Janeiro, *T. infestans* has been found [but whether infested or not is not mentioned].

H. Harold Scott

ABALOS, J. W. & WYGODZINSKY, P. Las Triatominae Argentinas (Reduviidae, Hemiptera). [**Argentine Triatominae**] *Universidad Nacional de Tucuman : Instituto de Medicina Regional. Publicación No. 601.* 1951, Monografía No. 2. 178 pp., 318 figs. (1 on pl.) [Bibliography.] English summary.

This useful monograph deals with the 17 species of Triatominae found in Argentina, which belong to 4 genera, *Triatoma*, *Neotriatoma*, *Panstrongylus* and *Psammolestes*. Of these, *Triatoma infestans* is most domestic in its habits, and most important in the spread of *Trypanosoma cruzi*. The first part of the monograph deals with this aspect of the Triatominae, including historical and folk lore references, biology in relation to Chagas's disease, and control methods. Illustration is by means of photographs, including clinical signs of Chagas's disease, the wild mammals which harbour *T. cruzi*, rural houses and animal quarters in which triatomids breed, and control measures in action. There is a chapter on methods of collecting and rearing Triatominae.

A detailed description of the general morphology, accompanied by figures, facilitates the use of the keys to the specific identification of the eggs and nymphs (first and fifth stage) and generic identification of the adults. Separate keys are given for the species of the genera *Triatoma* (11 species) and *Panstrongylus* (3 species). The individual species are dealt with in detail, covering external morphology, taxonomy, synonymy, and biology, and fully illustrated with photographs and drawings. The species of *Triatoma* may be divided into 3 groups based on the morphology of the genitalia and certain nymphal and adult characteristics. This sub-division is found to correspond with geographical distribution.

A commented bibliography completes the monograph. A. J. P. Goodchild

DE FREITAS, J. L. P. Reação de fixação de complemento para diagnóstico da moléstia de Chagas pela técnica quantitativa. [**Quantitative Complement Fixation Test for the Diagnosis of Chagas's Disease**] *Arquivos de Hig. e Saúde Pública.* S. Paulo. 1951, June, v. 16, No. 48, 55-94, 2 graphs. [46 refs.] English summary.

The author has divided this article into four chapters. The first briefly describes the preparation and standardization of the components of the reaction, the emulsion of sheep's corpuscles, the complement, etc., and the reading of the degree of haemolysis by a photo-electric colorimeter. The second details the mode of preparation and the standardization of the antigen. This has been detailed in an earlier paper [see this *Bulletin*, 1949, v. 46, 1129]. In chapter III, non-reacting and the titres of reacting sera, by varying the amount of complement or diluting the serum, are discussed. In the final chapter the author records the results of the test with reacting sera and, as controls, sera from patients with mucocutaneous leishmaniasis, syphilis, leprosy, pemphigus and vaccinia. Those desirous of details should consult the original; here we must rest content with summing up the results.

Trypanosoma cruzi was found in 86 patients whose sera were tested, 14 of them subacute or acute and 72 chronic. Of the former, 7 did not react, 5 had titres above 2.0 and two had titres below this, and the conclusion is stated that this c.f. test is not suitable for the diagnosis of such cases. Of the 72 chronic cases, the serum in one was non-reacting; in 70 the titre was over 1.9 and in the remaining one 1.8 [1.4 or less is regarded as indicating a negative].

Turning to the sera of patients with other diseases, there were 30 with mucocutaneous leishmaniasis; of these, 5 only reacted, with titres of 1.6, 1.7, 1.9, 2.0 and 2.0. It will be seen that all these were above 1.4 and the author states that in these 5 the possibility of infection by *T. cruzi* could not with

certainly be excluded. There were 46 sera from syphilitics. One had a titre of 1.9 and *T. cruzi* infection was possible here; another which reacted had had a positive xenodiagnosis. Of 31 leprosy patients (lepomatous form) none reacted; of 49 with pemphigus 45 were non-reacting; in the cases of the other 4 *T. cruzi* infection was possible. One of 17 vaccinia patients gave a reaction and in him a xenodiagnosis was positive. The very high titres were seen in those with cardiac forms of Chagas's disease.

H. Harold Scott

DE GÓES, P. & LOBO, M. B. Sobre o comportamento do anticorpo heterólogo ocorrente na doença de Chagas. [**The Behaviour of the Heterophile Antibody Occurring in Chagas's Disease**] *Anais Microbiol.* Rio de Janeiro. 1951, v. 1, 69-77. [11 refs.]

The English summary appended to the paper is as follows:—

"The occurrence of heterogenetic antibody in Chagas Disease has been reported in previous works. Since the nature of this antibody as well as its properties was not clear enough to allow separation from other similar antibodies occurring in other conditions (Forssman, infectious mononucleosis, epidemic hepatitis, etc.) we tried to study this subject further.

"Direct anti-sheep hemagglutination tests were made with sera of patients with Chagas Disease. The titres were generally high, being thus in accordance with the previous findings. The same sera were absorbed with several antigens (guinea-pig kidney, human liver, beef-heart, etc.) followed by hemagglutination tests.

"On the basis of the results obtained, the behaviour as well as the characteristics of this heterogenetic antibody of Chagas Disease were compared with those of similar antigens occurring in other conditions."

MORNET, P., LALANNE, A. & CISSOKO, M. Trypano-prévention chimiothérapique des zébus en A.O.F. [**Chemoprophylaxis of Trypanosomiasis in Zebu Cattle in French West Africa**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 1, 51-5.

LEISHMANIASIS

GVOZDENOVIĆ, M. & NEVENIĆ, V. Prilog proučavanju epidemiologije kala-azara. [**Study of the Epidemiology of Kala Azar**] *Higijena.* Belgrade. 1951, v. 3, No. 6, 412-18. French summary.

The authors, writing from Belgrade in 1950, examined 1,500 dogs in areas where human kala azar was endemic in the Lake Scutari region and the Montenegro littoral. They also examined 187 dogs from the Niš area. All the dogs were examined clinically and many were excluded as being healthy, but 305 were also examined by gland puncture, 520 by examination of blood from the saphenous vein and 79 (the most suspect) were chloroformed and smears taken from the spleen, liver and bone marrow. Leishman-Donovan bodies were not found in any case and in 520 specimens of blood examined by the formol-gel test, the results were also negative.

The authors conclude that the dog is not a reservoir for human kala azar in the regions surveyed.

H. J. O'D. Burke-Gaffney

PARROT, L. Notes sur les phlébotomes. LXIII.—Les phlébotomes de la ville d'Alger et de sa banlieue. [*Phlebotomus in Algiers and its Environs*] Arch. Inst. Pasteur d'Algérie. 1951, Dec., v. 29, No. 4, 300–304. [17 refs.]

Six species of *Phlebotomus* occur in Algiers and its environs. They are *P. perniciosus*, *P. sergenti*, *P. ariasi*, *P. perfiliewi*, *P. longicuspis*, and *P. minutus* var. *parroti*. The first 5 species named feed on warm-blooded animals, the sixth feeds exclusively on reptiles, especially the gecko (*Tarentola mauritanica*). A list is given of ten localities in and near Algiers, and the *Phlebotomus* species which have been recorded at those places. It has been demonstrated that *P. perniciosus* and *P. longicuspis* can transmit human and canine leishmaniasis. In the absence of *P. papatasi*, *P. sergenti* appears to be the most likely vector of oriental sore. *P. perfiliewi*, which transmits cutaneous leishmaniasis in parts of Italy, is too rare to be an important vector.

A. J. P. Goodchild

SEN GUPTA, P. C. & BHATTACHARYYA, B. The Spleen in Kala-Azar. *J. Indian Med. Ass.* 1951, Oct., v. 21, No. 1, 1–4, 6 figs. on 2 pls.

The histo-pathological changes in the spleen early in kala azar are not well known because a patient seldom dies in this stage of the disease. The authors describe the histo-pathological changes in a case in which they believe that the disease was in its early stages on account of the similarity of the changes with those found in the hamster 90 days after it had been infected; they suggest that the duration in this case was 3 to 4 months.

The capsule and trabeculae were normal. The lymph follicles were invaded by parasite-laden "clasmatoocytes"; in the "pulp" there were many parasitized "clasmatoocytes", few of which also contained ingested red cells, lymphocytes and plasma cells. There was reticulo-endothelial proliferation in the sinuses, which were consequently narrowed.

In "chronic kala azar" (that is in the later stages of the normal course of untreated kala azar) the capsule and trabeculae are thickened. The lymphoid follicles show increased reticulum, and the sinuses are congested and widely dilated. The pulp is congested and there are numerous parasitized macrophages which may also contain blood cells, in both the pulp and the sinuses.

In the very advanced stages there is gross thickening of the capsule and trabeculae which consists mainly of fibrous tissue, and even greater dilatation of the sinuses and congestion of the pulp. The lymphoid follicles are now inconspicuous.

The authors discuss the functions of the spleen, particularly with reference to the stages of kala azar. There are three functional elements in the spleen, the vascular system, the reticulo-endothelial tissue and the lymphoid tissue. In the early stages of kala azar the vascular changes are minimal, but there is considerable reticulo-endothelial activity, although only a few macrophages contain blood cells. This stage is associated with "a mild degree of leucopenia and anaemia that may well be due to the characteristic changes in the bone-marrow in kala-azar". Later, there is an increase of vascular bed in the spleen and increased activity of the macrophages, at which stage there is evident hypersplenism which accounts for the anaemia, leucopenia and thrombocytopenia. Specific treatment at this stage causes a reversal of these conditions.

In the very advanced stage this hypersplenism is even more evident, but the structural changes in the spleen are now so extreme that complete reversal does not always follow specific therapy and although the parasitic stimulus

to macrophage proliferation has disappeared the vascular congestion still remains ; this causes changes in the blood cells which stimulate phagocytosis so that proliferations of reticulo-endothelial tissue still continues and a vicious circle is established resulting clinically in splenomegaly and anaemia [a sequel to kala azar described by the reviewer in 1927].

L. E. Napier

PORTIER, A., BOULARD, C. & MASSONNAT, J. Accident polynévritique après une cure de 2168RP pour Kala Azar de l'adulte. [**Polynuritic Lesion after Treatment of Kala Azar in an Adult with 2168RP (Glucantime)**] *Algérie Méd.* 1951, Feb., v. 55, No. 2, 674-7.

LEFRANC, M. Cinq cas de leishmaniose cutanée observée à Alger. [**Five Cases of Cutaneous Leishmaniasis Seen in Algiers**] *Algérie Méd.* 1951, May, v. 55, No. 5, 907-8.

FEVERS OF THE TYPHUS GROUP

GREIFF, D. & PINKERTON, H. **Rickettsiostasis in Fertile Eggs from Use of Antibiotic Residues in Poultry Feeds.** *Proc. Soc. Exper. Biol. & Med.* 1951, Dec., v. 78, No. 3, 690-92.

The authors found that no rickettsial growth occurred in the eggs of hens that had been fed for 3 weeks on a diet to which had been added 1.0 per cent. of a mash remaining over after the extraction of aureomycin or terramycin and containing 1.0 gm. or more of the antibiotic in each pound.

These residues from the manufacture of antibiotics are now extensively used as growth promoters by chicken farmers in the U.S.A. so that laboratories will have to stipulate that eggs bought for yolk-sac culture should be from fowls to which these substances have not been given.

John W. D. Megaw

ONUL, B. Weil-Felix-Reaktion bei Typhusinfektionen im Laboratorium. [**The Weil-Felix Reactions in Laboratory Infections with Typhus Fever**] *Acta Med. Turcica.* 1951, Jan., v. 3, Nos. 3/4, 35-8.

Examples are given of laboratory infections with louse-borne typhus in which the Weil-Felix reactions were at unusually low titres.

Among 19 patients attacked in a laboratory outbreak most cases remained negative in the second and third weeks. It is suggested that previous inoculation interfered with the development of immune bodies.

The reactions observed in healthy persons after primary and secondary inoculations are of interest. Among 66 persons the titres 5 months after inoculation were :— 1-200 in 36 ; 1-100 in 18 ; 1-50 in 10 and zero in 3.

Inoculation was repeated 6 months later and after an interval of 2 weeks the titres were :— 1-400 in 55 ; 1-200 in 6 ; 1-50 in 3 and zero in 2.

John W. D. Megaw

WILLSCH, G. Spätrezidive nach Fleckfieber. [**A Late Relapse of Typhus Fever**] *Med. Klin.* 1952, Feb. 29, v. 47, No. 9, 273-5. [13 refs.]

A patient who had suffered from typhus fever in Russia in 1942 was treated for a relapse of the Brill type in 1950. The Weil-Felix reaction was positive in rising titre ; the rickettsia-agglutination and complement-fixation reactions with *Rickettsia prowazeki* antigen were strongly positive.

The author expresses the opinion that in all cases of typhus fever, however mild, aureomycin or chloramphenicol should be given during or after the illness with a view to eradicating the infection and preventing the late relapses which are believed to cause recrudescence of the disease after inter-epidemic periods.

[Some observers suspect that the antibiotics are more likely to promote than prevent the occurrence of the carrier state ; their action is rickettsiostatic, not rickettsiocidal, and their early administration in cases of scrub typhus has been found to be followed by numerous early relapses which suggest that they interfere with the development of solid immunity.] *John W. D. Megaw*

MURRAY, E. S., OFSTOCK, A. & SNYDER, J. C. **Antibody Response of Human Subjects to Epidemic Typhus Vaccine Three to Eight Years after Previous Immunization.** *J. Immunology.* 1952, Feb., v. 68, No. 2, 207-18. [15 refs.]

In this investigation 17 volunteers were given single injections (1.0 ml.) of anti-typhus vaccine 4 to 6 years after the last previous vaccination, which in 13 cases was also the only one.

The complement-fixation response was prompt ; by the 10th day the geometric mean titre was 1-125.2 and this was 8 to 32 times higher than the mean titres observed in three groups of persons after primary vaccination with the usual two doses. The titres after the booster injections reached their peak about the 9th or 10th day ; by the 40th to the 60th day they had fallen to one-half or one-quarter of the maximum level. A second booster dose given 6 to 8 weeks after the first caused no further rise in the titre.

In primary vaccination it was found that the titre was higher when the interval between the two doses was increased to 17 days, and still higher when it was 27 days ; an interval of 2 to 4 weeks between the two doses is therefore considered desirable. *John W. D. Megaw*

KITAOKA, M., TAKEMORI, N., SHISHIDO, A. & JO, K. **On Epidemiology of Murine Typhus in Saitama 1948, in Niigata 1949 and Multiple Occurrence of Murine Typhus in one Family.** *Japanese Med. J.* 1951, June, v. 4, No. 3, 143-55, 2 figs. [33 refs.]

The authors describe the investigation by modern methods of several outbreaks of flea-borne typhus in various areas in Japan. The largest was one in which 20 cases occurred sporadically in 6 villages in the Saitama Prefecture in the months of October, November and December, 1948. This was of special interest in that it followed closely on a local campaign of rat trapping and killing in the affected area and no simultaneous effort was made to control the rat fleas by DDT ; the authors point out the necessity for combined control of the rats and their fleas.

The outbreak was at first regarded as one of louse-borne typhus, but the complement-fixation reactions pointed strongly to infection with *Rickettsia typhi* [*R. mooseri*], and in 3 cases this organism was isolated and identified. Among 19 patients tested, the complement-fixation reaction was positive with murine antigen at titres two or more times higher than with louse-borne typhus antigen in 13 cases and in only one case were the titres equal.

The almost simultaneous occurrence of 3 cases in one family in a village near Tokyo is described ; the patients were attacked within a period of 3 days in late January 1950, and an epidemic of louse-borne typhus had broken out in Tokyo early in the same month so that the outbreak was regarded as being due to *R. prowazeki* infection till the complement-fixation tests showed the disease to be murine.

Three other outbreaks are reported in which 2 or 3 members of one household were attacked almost simultaneously and the infection was found to be of the murine type. References are given to many reports of similar family outbreaks of the same kind in Japan, including one in which 10 cases occurred in the same family during a period of 2 months.

The occasional occurrence of "strong cross reactions" with the two kinds of rickettsiae is not regarded as evidence of the existence of an intermediate form of typhus.

The rickettsia-agglutination test was found helpful in the few cases in which it was done.

John W. D. Megaw

KUWATA, T. **Analysis of Immunity in Experimental Tsutsugamushi Disease.** *J. Immunology.* 1952, Feb., v. 68, No. 2, 115-20. [22 refs.]

Mice immunized by a living strain of *Rickettsia tsutsugamushi* of low virulence were challenged at varying intervals with a living strain of high virulence. The mice challenged 4 days after the original injection were as susceptible as control mice; those challenged after 8 days had a definite degree of resistance and mice challenged after the 20th day were highly resistant, yet suspensions of their tissues were highly lethal for normal mice so that superinfection with the virulent strain had obviously occurred. The super-infecting strain persisted for a long time, in one case up to 180 days, in the tissues of the mice.

After primary immunization with the highly virulent strain superinfection still occurred when the mice were challenged later with the same strain even when the challenging dose was as small as 10 LD₅₀.

The author concludes by stating:—"Why immunized and highly resistant mice can not eliminate persisting rickettsiae from tissues awaits further investigation."

John W. D. Megaw

FENATI, S. L'aureomicina nella cura della febbre eruttiva mediterranea. [**Aureomycin in the Treatment of Boutonneuse Fever**] *Ann. d. San. Pubblica.* Rome. 1951, Nov.-Dec., v. 12, No. 6, 2181-6. [34 refs.]

The English summary appended to the paper is as follows:—

"The author, after a brief review of the literature concerning the modern antibiotics therapy against rickettsial diseases, refers to the brilliant results obtained with aureomycin in 5 cases of Mediterranean Eruptive Fever."

GELFAND, M. **A Case of Tick Bite Fever in an African.** *East African Med. J.* 1952, Jan., v. 29, No. 1, 30-31.

Most of the cases of tick bite fever recorded from Africa seem to refer to European subjects. The author and others have watched for some years, unsuccessfully, for signs of this condition in the African. He now records in some detail a typical case in an African of 25 from Portuguese East Africa, who had been in Southern Rhodesia for some time. The case showed the classical features, including the eschar, regional lymphadenitis and typical rash. *Proteux OXK* agglutination was positive at 1/40. Rapid recovery followed treatment with chloramphenicol.

The author notes that it is difficult to account for the apparent rarity of the disease in Africans, whose rural living conditions expose them greatly to the tick. It has been suggested that it is contracted in infancy when the symptoms

are so mild that the patient is not brought to hospital : but the author observes, on the other hand, that African children are, in fact, frequently brought to hospital for mild complaints.

H. J. O'D. Burke-Gaffney

ORMSBEE, R. A. **The Growth of *Coxiella burnetii* in Embryonated Eggs.** *J. Bacteriology.* 1952, Jan., v. 63, No. 1, 73-86, 4 figs. [14 refs.]

By experiments of which full technical details are given, the author has found that a progressive increase in the number of rickettsiae in infected yolk sacs occurs so long as the embryo survives, but multiplication ceases on the death of the embryo. Growth of the rickettsiae was restricted to the yolk sac ; none occurred in the other tissues of the embryo.

The number of rickettsiae present at each stage was estimated by finding the number of complement-fixing units contained in a given quantity of suspension of yolk sac or other tissues.

The maximum yield of rickettsial antigen can be obtained by collecting and harvesting at one time the yolk sacs of all eggs in which death occurs during the 4-day period after 50-60 per cent. of the embryos have died. The yolk sacs of any eggs still alive are added.

John W. D. Megaw

BABUDIERI, B. & MOSCOVICI, C. **Experimental and Natural Infection of Birds by *Coxiella burnetii*.** [Correspondence.] *Nature.* 1952, Feb. 2, 195-6.

Among the various experiments described the following are of special interest. Twelve pigeons were given by the oral route a few drops of yolk-sac suspension of *Coxiella* [*Rickettsia*] *burnetii*. After 15 days one pigeon had a complement-fixation titre of 1-16 and 3 others had titres of 1-4 to 1-8. On the 26th day another reacted at 1-16. Kidney suspensions made from some of the pigeons 40 days after inoculation were injected intraperitoneally into guineapigs some of which gave positive fixation reactions a month later.

None of 28 pigeons or other birds from uninfected localities gave positive reactions, but among 32 pigeons, 3 chickens and 1 goose from places known to be foci of Q fever one of the pigeons reacted at 1-64 and 3 others at 1-8 ; the goose reacted at 1-64. The pigeon that reacted at 1-64 gave a negative reaction 130 days later but a suspension of its kidneys caused a positive reaction in an inoculated guineapig.

The authors think that pigeons and other birds may play important parts in transmitting infection because of their habit of feeding on the droppings of mammals.

John W. D. Megaw

LASS, R. Qu-Fieber in Oesterreich. [**Q Fever in Austria**] *Wien. klin. Woch.* 1952, Feb. 29, v. 64, No. 9, 159-62. [22 refs.]

The author, apparently in all seriousness, explains the name "Qu-Fieber" as an abbreviation of Queensland or "querry" fever and states that the designation querry fever, *i.e.* stable fever, is suitable because farmyard animals are the special sources of infection.

Among 360 cases personally observed since 1948, complement-fixation tests were made on 100 patients, of whom only 24 reacted at titres of 1-16 to 1-40 and 16 at 1-8 to 1-10. The stage of the illness at which the tests were made is not stated. The clinical picture was the same in the negative as in the positive cases. In 70 per cent. of the cases the illness was prolonged and was characterized by undulant recurrences of mental depression.

Great loss of weight, often up to 20 kgm., was usual. The onset was sudden ; in most cases there was an initial spell of fever lasting 4-10 days, and only about 25 per cent. of the patients had no relapse. A girdle pain at the level of the diaphragm occurred in 42.5 per cent. of the cases.

Aureomycin was given to 53 patients, with uniformly excellent results.

John W. D. Megaw

FELLERS, F. X. **An Outbreak of Q Fever. I. Clinical Study.** *U.S. Armed Forces Med. J.* 1952, Feb., v. 3, No. 2, 287-95, 4 figs. [10 refs.]

In February and March, 1951, there was an explosive outbreak of Q fever among men of the U.S.A. Air Force stationed in Tripoli. Of the 25 patients 23 had been living in one barrack and the other 2 lived nearby.

The clinical features were of the usual type. Radiological evidence of pneumonitis was seen in 20 of the patients, an exceptionally high proportion which, judging by the remarkably clear definition of the two photographs reproduced, may have been accounted for by the high standard of the radiological examination.

The complement-fixation reactions were slow in appearing ; in the 3rd week only 5 were positive, at low titres of 1-10 to 1-40 ; by the 7th week 16 had reacted and in the 12th or 13th week 4 more reacted. Two remained negative throughout the period of observation.

John W. D. Megaw

BAYLON, H., BLOCH, F., GIROUD, P. & COUMEL, H. Au sujet des manifestations cardiovasculaires des rickettsioses et de leur évolutivité. [**The Evolution of the Cardiovascular Manifestations of Rickettsial Diseases**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1952, Nos. 1/2, 67-72.

A case is described in which a chronic low-grade endocarditis and an arteritis affecting the left radial and the right posterior tibial artery were suspected of having resulted from a previous attack of louse-borne typhus. The evidence in support of this view was that the patient had made a long stay in North Africa where typhus fever was endemic, that a serum-protection test for typhus fever was strongly positive, and that considerable benefit followed a course of treatment by aureomycin, terramycin and chloramphenicol. On the other hand there was no evidence that the patient had actually suffered from typhus and a rickettsia-agglutination test for louse-borne typhus was negative. An unexpected finding was a strongly positive rickettsia-agglutination test for Q fever with a titre rising to 1-3,220 and falling later to 1-20. There was no clinical evidence of the occurrence of Q fever.

John W. D. Megaw

ORMSBEE, R. A. & PICKENS, E. G. **A Comparison by means of the Complement-Fixation Test of the Relative Potencies of Chloramphenicol, Aureomycin, and Terramycin in Experimental Q Fever Infections in Embryonated Eggs.** *J. Immunology.* 1951, Nov., v. 67, No. 5, 437-48, 3 figs. [15 refs.]

In this investigation the effects of aureomycin, chloramphenicol and terramycin against the Nine Mile strain of Q fever (*Rickettsia burneti*) in chick embryos were compared by means of the complement-fixation test and direct microscopic examination. Six-day-old egg embryos were injected *via* the yolk sac with 0.5 ml. quantities of a standard 10 per cent. yolk sac suspension of *R. burneti* of such potency that approximately 80 per cent. of the untreated embryos were dead 7 days later. Twenty-four hours later 0.5 ml. of antibiotic in saline or saline alone was injected by the same route. Deaths occurring

within 48 hours were regarded as due to trauma. From the 3rd or 4th day onwards 2 or 3 living embryos from each group were killed daily, the yolk sacs harvested, washed in cold 0.87 per cent. NaCl, weighed and blended 1 minute in a Waring blender in cold 0.87 per cent. saline to make a final yolk sac preparation of 10 per cent. The yolk sacs of dead embryos were similarly treated. The 10 per cent. yolk sac preparations were centrifuged at 1,000 r.p.m. for 10 minutes, the fat and sediment discarded and the remaining suspension extracted with 2 to 3 volumes of ethyl ether. The resulting aqueous phase was the final preparation of antigens used for the complement-fixation test. Each preparation was titrated against 3 or 4 standard Q fever antisera and an average titre was calculated. Full details of the method are described elsewhere (1951, in the press). The total N was measured by the micro-Kjeldahl method and complement-fixation results were expressed in terms of complement-fixing units (CFU) per mgm. N. The CFU/mgm. N value was taken as a measure of the concentration of rickettsiae in the tissue. Smears were also made from all yolk sacs and the numbers of rickettsiae seen were roughly estimated.

In untreated controls the complement-fixation test first became positive on the 4th day. *R. burneti* was first seen in smears on the 3rd day. Preliminary experiments showed that the CFU/mgm. N was a measure not only of the rickettsial antigen present but also indirectly of the number of organisms per unit of host protein.

The antibiotic effects were first compared in terms of the delay in occurrence of positive CF values. By this means the compounds in descending order of effectiveness were as follows:—terramycin > aureomycin > chloramphenicol > penicillin G. The effects were then compared according to rate of increase of CF values. In controls the first three positive results were 10, 85 and 192 on the 4th, 5th and 6th days. Treatment with 0.25 mgm. terramycin, however, gave levels of 13, 10 and 22 on the 13th, 14th and 15th days. Similar results occurred with 1 mgm. aureomycin, 1 mgm. chloramphenicol, 5 mgm. streptomycin and "possibly" 6 mgm. penicillin. When the compounds were compared with the use of an equimolar dose of 4 to 5×10^{-4} mM, chloramphenicol prevented the appearance of a positive complement-fixation titre for 1 day, aureomycin for 4 days and terramycin for 10 days.

Mary Barber

RABIES

REAGAN, R. L. & BRUECKNER, A. L. **Effect of Rabies Street Virus in the Cotton Rat and the Swiss Albino Mouse.** *Proc. Soc. Exper. Biol. & Med.* 1951, Dec., v. 78, No. 3, 702-3.

Cotton rats and Swiss albino mice were infected by various routes with a street virus strain V 308, which had been isolated from dog brain and passaged twice in mice and once in cotton rats intracerebrally. Infection resulted in both species by injection of 0.1 ml. of a 10 per cent. infected cotton-rat brain suspension titring $10^{4.5}$ in cotton rats and $10^{4.2}$ in mice, after intraperitoneal, intradermal, intramuscular, intralingual and intracardiac injections: 3 animals were used for each route. Swiss mice also contracted histologically verified rabies by the instillation of 0.1 ml. of the same suspension intranasally, intrarectally and orally, while cotton rats could not be infected by the intranasal route.

C. Klimt

LÉPINE, P. & ATANASIU, P. Sur la virulence par voie sous-cutanée du virus fixe (souche Pasteur) pour la souris, le hamster, le cobaye et le lapin.

[**Virulence of the Pasteur Fixed Strain of Rabies Virus for Mice, Hamsters, Guinea-pigs and Rabbits by the Subcutaneous Route**] *Ann. Inst. Pasteur.* 1951, Aug., v. 81, No. 2, 213-17. [12 refs.]

Serial intracerebral (i.c.) passages of the Pasteur fixed strain of rabbit-passaged rabies virus were made in mice with the use as a starting material of a strain which had been passed for 65 years a total of 1,782 times in rabbits. At the first mouse passage the i.c. titre in mice was $10^{-3.5}$ which was similar to that which had been obtained many times in mice with this strain of virus. With serial mouse-to-mouse passage (of mouse-brain virus) the LD₅₀ increased to $10^{-5.5}$ by the seventh passage, and reached $10^{-7.5}$ by the tenth passage. At the twentieth passage the virus with a titre of $10^{-7.5}$ was lyophilized and after four months storage the titre was found to be $10^{-6.5}$.

Thirtieth passage (titre $10^{-7.5}$) virus was found to have a titre of $10^{-3.62}$ when inoculated in 0.1 ml. quantities subcutaneously (s.c.) into mice (age or strain not stated). Hamsters, *Cricetus auratus*, were also highly susceptible to s.c. inoculation of the virus and titres of 10^{-5} were obtained. In guinea-pigs and rabbits the titre by the s.c. route was $10^{-3.5}$. Rabbits inoculated subcutaneously with 10^{-3} dilutions of the mouse-passaged virus presented symptoms like those of furious rabies after a short incubation period.

In all animals the pathological changes were similar to those produced by fixed rabies virus and typical Negri bodies could be found particularly in mice.

[The authors omit to state that the high-titre mouse-passaged virus was immunologically similar to the virus from which it was originated.]

G. W. A. Dick

GARRISON, S. C. **Encephalomyelitis complicating Antirabies Vaccination treated with Cortisone.** *Amer. J. Med.* 1952, Jan., v. 12, No. 1, 135-6.

"A case of encephalomyelitis complicating antirabies vaccination is reported in which there appeared to be a dramatic response to cortisone therapy."

AMERICAN J. OF MED. 1951, Aug., v. 11, No. 2, 228-9. Discussion 229-36, 4 figs. **Fatal Reaction to Antirabies Vaccine.** [Clinico-pathologic Conference (Washington University School of Medicine).]

This is a clinical and pathological discussion of a number of aspects of the rabies problem around one fatal case presumably due to anti-rabies vaccination. Death occurred on the 15th day after exposure to a suspect dog's saliva on a wound more than 3 days old, after a full course of 14 anti-rabies injections. [The type of vaccine used was not stated.] This subject ought not to have been vaccinated at all, particularly considering the patient's previous history of bronchial asthma.

Pathologically this was not a case of demyelinating encephalomyelitis, but rather one of polyradiculo-neuritis of the Guillain-Barré type, which, experimentally at least, has so far not been connected with paralysis following anti-rabies vaccination.

C. Klimt

KOPROWSKI, H. & COX, H. R. **Recent Developments in the Prophylaxis of Rabies.** *Amer. J. Pub. Health.* 1951, Dec., v. 41, No. 12, 1483-9. [19 refs.]

This is a discussion of the recommendations of the World Health Organization's Expert Committee on Rabies and some of the criticisms raised against them. [See this *Bulletin*, 1951, v. 48, 32.]

C. Klimt

PLAGUE

MARTÍN SANZ, L. Peste bubónica. [Bubonic Plague] *Med. Colonial*. Madrid. 1952, Mar. 1, v. 19, No. 3, 263-77.

A general review.

POLLITZER, R. **Plague Studies. 2. The Plague Bacillus.** *Bull. World Health Organization*. Geneva. 1952, v. 5, No. 1, 73-108. [181 refs.]

This is a critical and fully documented summary of the contributions to knowledge of *Pasteurella pestis* that are included under the following headings ; (1) morphological characteristics, (2) cultural characteristics, (3) biochemical properties, and (4) vital resistance.

The list of 181 references to the literature is sufficient evidence of the comprehensive nature of this study, the second of a series which, when complete, will form a manual on plague to be published as a Monograph of the World Health Organization. [For part 1, see this *Bulletin*, 1952, v. 49, 388.]

John W. D. Megaw

BOIRON, H. La révolution à Dakar. [The "Revolution" at Dakar] *Bull. Méd. de l'Afrique Occidentale Française*. 1951, v. 8, No. 2, 185-90.

Whereas, in the years previous to the recent war, domestic fleas were abundant in the region of Dakar, control measures with DDT had by 1946-7 succeeded in reducing the flea population almost to nothing. Since 1951 however, the domestic flea populations have begun to increase. In order to interpret this, the author has consulted past records of large numbers of fleas, examined by members of the Pasteur Institute and others. He finds that, in past years, the commonest human flea was *Synosternus pallidus*, normally a parasite of rodents and small carnivores, while *Pulex irritans* was not recorded with certainty. Since 1949, *P. irritans* has appeared, and increased in numbers in both rat and domestic collections, while *S. pallidus* has almost disappeared. The author does not form any definite conclusions as to the ecological mechanism at work, and whether it is entirely due to greater resistance to insecticides by *Pulex* or whether the absence of competition from *Synosternus* also plays a part.

A. J. P. Goodchild

BAKER, E. E., SOMMER, H., FOSTER, L. E., MEYER, E. & MEYER, K. F. **Studies on Immunization against Plague. I. The Isolation and Characterization of the Soluble Antigen of *Pasteurella pestis*.** *J. Immunology*. 1952, Feb., v. 68, No. 2, 131-45, 5 figs. [24 refs.]

This study is of a highly technical nature ; an adequate summary would be of interest only to workers specially interested in the subject, and they will desire to read the original paper.

The authors describe the isolation and characterization of two antigenic fractions from the water-soluble portion of *Pasteurella pestis* which was obtained by extracting acetone-killed cultures with neutral salt solution. One of the fractions, "IA", was precipitated by ammonium sulphate ; it contained carbohydrate in addition to the specific protein element and occurred as a viscous substance which could not be crystallized ; the other fraction, "IB", was obtained by purification of the IA fraction, it was free from carbohydrate and could be isolated as crystals ; otherwise the two fractions had similar immunizing and other properties. Both fractions acted as potent antigens for immunizing mice and rats, but had little immunizing action on guineapigs,

and both were non-toxic. In addition to these fractions the water-soluble extract of *P. pestis* contained a toxic substance which was separated and concentrated but not yet purified and characterized.

The water-insoluble residue of the bacilli contains antigenic substances which, unlike the water-soluble antigens, produced a relatively high degree of immunity in guineapigs.

The authors refer to the antigenic fractions of *P. pestis* described by SEAL [see this *Bulletin*, 1952, v. 49, 138, 139]; they consider that these have not been adequately characterized, but they admit that further study of the problem is needed.

John W. D. Megaw

CHEN, T. H., QUAN, S. F. & MEYER, K. F. **Studies on Immunization against Plague. II. The Complement-Fixation Test.** *J. Immunology*. 1952, Feb., v. 68, No. 2, 147-58, 1 fig. [27 refs.]

A complement-fixation test is described in which the antigen is one of the "I" fractions [presumably "Fraction IB"] referred to in the previous paper. A specific high-titre anti-plague serum is used as the standard antibody. The titres observed were generally in direct proportion to the results obtained with precipitin, agglutination, immunization, and mouse-protection tests.

Examples are given of the practical application of the test. Three sera from persons convalescent from plague were examined; titres of 1-32; 1-64 and 1-16 were observed on the 18th, 36th and 44th days respectively, so that, contrary to the accepted opinion, the test is of value in retrospective diagnosis.

In the application of the test to the estimation of the value of plague vaccines an interesting finding was "the superior immunogenic power of the present plague vaccine produced at the Haffkine Institute in Bombay". The Haffkine vaccine gave a titre of 1-1,024; the "Cutter vaccine, Army issue" [which is presumably the U.S.A. Army vaccine] gave a titre of 1-128 and the "Hooper Foundation standard antigen (1950)" one of 1-32.

Other applications of the test are suggested; estimation of the potency of anti-plague sera, the recognition of *P. pestis*, and the diagnosis of plague in dead wild rodents by testing extracts of the tissues even when obtained from dried or decomposed animals.

The availability of Fraction IB in crystalline form as an antigen is regarded as insuring uniformity in the findings.

John W. D. Megaw

GIRARD, G. Dépistage post mortem de la peste par ponctions d'organes.

Trente années d'expériences à Madagascar. [**Post-Mortem Diagnosis of Plague by Puncture of Organs: 30 Years' Experience in Madagascar**] *Bull. World Health Organization*. Geneva. 1952, v. 5, No. 1, 109-16.

The author describes and strongly recommends a method of detecting plague infection by examination of serous fluid obtained by post-mortem puncture with a hypodermic syringe, of the liver, lungs (3 punctures on each side) and the bubo when this is present. Smears of the fluid are made on glass slides and stained by Gram's method; the rest of the fluid is mixed with 2.0 ml. normal saline in which the bacilli remain viable for about 10 days at 20-24°C. and for a long time at 4.0°C.; guineapigs are inoculated by rubbing this mixture on the shaven and slightly excoriated skin.

By the systematic adoption of the method, 6,114 cases of plague have been detected in Madagascar from 1931 to the end of 1949; during the same period only 1,028 cases were diagnosed before death.

Among 4,385 cadavers tested in both of the above ways the results obtained were:—781 were positive by the smear test, and of these 88.3 per cent. were

positive by inoculation ; 962 were suspected by the smear test and 42.5 per cent. of these were positive by inoculation ; 2,642 were negative by the smear test and 4.7 per cent. of these were positive by inoculation.

Among 678 cases in which the inoculation test alone was done 13.9 per cent. were positive. [For the author's original description of these methods, see this *Bulletin*, 1937, v. 34, 789 ; 1939, v. 36, 310.] *John W. D. Megaw*

RAMACHANDRAN, K. **Treatment of Plague with Aureomycin.** *J. Indian Med. Ass.* 1952, Feb., v. 21, No. 5, 217-18.

The author treated 15 cases of plague with aureomycin by mouth in a hyperendemic area of plague in Hyderabad State.

Diagnosis was made on clinical features and on the epidemiological history [no mention is made of bacteriological examination]. There were 12 cases of bubonic plague and 3 of septicaemic. The ages of the patients varied from 6 to 35 years.

Three of the patients (including two with septicaemic plague) were very ill on admission and died within a few hours. The remainder were cured. The dose of aureomycin was 250 mgm. every 6 hours or 500 mgm. every 2 hours, according to the case. The total amount of aureomycin given varied from 2.5 to 7.5 gm. in the successful cases : in the three patients who died, there was only time for a few doses to be given. The temperature became normal in 3 to 7 days. No toxic effects of the drug were seen.

Full details of the patients are given in a table. *H. J. O'D. Burke-Gaffney*

CHOLERA

BLASS, Judith, LECOMTE, Odette & MACHEBOEUF, M. Recherches sur les amino-acides libres de *Vibrio cholerae* par microchromatographie. [**Microchromatographic Study of the Free Amino-Acids of *Vibrio cholerae***] *Bull. Soc. Chimie Biol.* 1951, v. 33, No. 10, 1552-6, 2 figs. [14 refs.]

DE, S. N., SARKAR, J. K. & TRIBEDI, B. P. **An Experimental Study of the Action of Cholera Toxin.** *J. Path. & Bact.* 1951, Oct., v. 63, No. 4, 707-17, 4 figs. on 2 pls. [22 refs.]

The pathological effects produced by the intraperitoneal injection of a *V. cholerae* suspension in rabbits were investigated, the material used for the purpose being a heat-killed suspension of washed vibrios at a concentration of 100 million organisms per ml. One ml. of the suspension per kilogramme, killing in 2 hours, was taken as the minimum lethal dose.

The injection was followed by a fall in blood pressure which commenced within half an hour and continued to death. Haemoconcentration was also produced. There was an outpouring of fluid rich in protein and poor in cells in the peritoneum, and when Evans blue was injected intravenously the fluid was deeply stained. The submucous and serous coats of the small intestine were oedematous and also the stroma of the mucous membrane, but the epithelium was normal. Evans blue staining of the coats and of the intestinal contents was marked. There was oedema of the myocardium with swelling and granular degeneration of the muscle fibres and loss of striation.

The kidneys showed characteristic changes. After a minimum lethal dose the cortex was extremely pale, while the medulla and the boundary zone showed a dark dusky red colour macroscopically. Ischaemia of the cortical

glomeruli, and poor vascularity around the cortical tubules were seen. The cortical glomeruli were collapsed and the spaces of Bowman's capsule and tubular lamina were non-existent. In contrast the glomeruli of the boundary zone were congested and the capillary tufts were open and full of blood cells. The peri-glomerular tubules showed granular and more eosinophilic cytoplasm. In the medulla there was intense congestion of the vasa recta and the cells of the limbs and loops of Henle were swollen and granular. When heavy doses of the "toxin" were used the appearances were different. The cortex was very congested and the cortical peri-glomerular tubule showed parenchymatous degeneration similar to that in the medullary and juxta-medullary tubules.

Comparative observations were made with rabbits given hypertonic glucose solution subcutaneously to study the effect of simple dehydration. This produced considerable haemoconcentration within 3 hours, but with a small and less regular fall in blood pressure. The organs appeared congested, and the cut surface of the kidney showed a uniform congestion without the contrast between the cortex and medulla produced by the cholera toxin. No other microscopic abnormality was shown in the organs.

The injection of a similarly prepared "typhoid toxin" produced a fall in blood pressure without haemoconcentration. There was no free fluid in the peritoneal cavity or other macroscopic change. The kidney showed uniform congestion and cloudy swelling of the tubular epithelium in both cortex and medulla. There was no oedema of the myocardium or intestinal coats, but the heart muscle showed some granular degeneration.

The fall in blood pressure after injection of the "cholera toxin" is attributed partly to the degree of haemoconcentration produced by leakage into the peritoneum and elsewhere and partly to its action on the cardiovascular system. An alteration in the permeability of the capillaries appears to be produced by the action of the "toxin" which allows the passage of plasma-like fluid into the tissues. The changes in the kidney result in a diversion of the toxin-laden blood from the cortex to the medulla, the cortical glomeruli and tubules being thus partly protected from the action of the toxin. As the majority of the glomeruli are rendered ischaemic further loss of body fluid is prevented. This mechanism fails when a very heavy dose of the toxin is given and irreversible damage to the cortical parenchyma may occur, leading to uraemia.

J. Taylor

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

RADKE, R. A. **Incidence of Amebiasis in Korean Veterans.** *U.S. Armed Forces Med. J.* 1952, Feb., v. 3, No. 2, 323.

Ninety-three soldiers recently returned from active service in Korea and admitted to a U.S. Army hospital with malaria, were examined by sigmoidoscope: 47 were positive for *E. histolytica*. In 50 of the cases, microscopic examinations were made of 3 stools taken after saline purge. It was found that 23 of these were positive by sigmoidoscopy only, 3 by stool examination only and 7 by both methods.

The author draws attention to the need for using every available means for demonstrating *E. histolytica* when its presence is suspected. He observes that amoebiasis "is a disease of military significance in the Korean campaign", but adds that these men had been in actual combat, under conditions less sanitary than those of the supporting troops.

H. J. O'D. Burke-Gaffney

RAGUSA, G. Il quadro ematico nelle epatiti amebiche. [**The Blood Picture in Amoebic Hepatitis**] *Acta Med. Italica*. 1951, Nov., v. 6, No. 11, 293-7. [21 refs.] English summary (9 lines).

The author reviews the literature on the subject and then discusses the results of blood examination in 46 cases of amoebic hepatitis, mostly liver abscess, treated in the teaching hospital of Catania in 1939-1950.

A wide variety of factors may influence the blood picture in this disease, such as toxic substances produced either by the parasite or from the disintegration of liver tissue, and the condition of the blood-forming organs as affected by the duration of illness, the patient's state of immunity and his diet.

Most of the cases showed a hypochromic anaemia and a leucocytosis, and the leucocyte count can provide useful information in both diagnosis and treatment of this condition. J. Cauchi

OPENSHAW, H. T. & WOOD, H. C. S. **Studies of the Structure of Emetine. Part V. The Structure of the Rubremetinium Salts.** *J. Chem. Soc.* 1952, Feb., 391-8, 3 figs.

LINDSAY, A. E., GOSSARD, W. H. & CHAPMAN, J. S. **Treatment of Unusual Pulmonary Amebic Abscess with Chloroquine.** *Dis. of Chest*. Chicago. 1951, Nov., v. 20, No. 5, 533-8, 5 figs.

"A case of pulmonary amebic abscess of the right upper lobe with amebic hepatitis is reported in which hematogenous spread of the amebic parasites from liver to lung was the most probable pathogenetic likelihood. Since Emetine alone failed to cause a satisfactory response, and Chloroquine induced complete clinical remission, it is felt that Chloroquine is a useful agent in cases of pleuro-pulmonary amebiasis."

HALAWANI, A., ABDALLAH, A. & EL KORDY, M. I. **Resotren ; a New Therapeutic Agent for Amoebiasis ; a Preliminary Report.** *J. Roy. Egyptian Med. Ass.* 1951, v. 34, Nos. 11/12, 731-4.

"Resotren is a halogen quinoline derivative" not readily soluble in water, manufactured by Bayer in Germany. Its precise structure is not stated. It is claimed by the makers that when swallowed the drug breaks up into two portions ; one of these is readily absorbed, the other is not. Both portions are amoebicidal ; thus the drug can act both on intestinal and on extra-intestinal amoebic infections. The drug has proved to be remarkably free from toxicity.

Fifteen Egyptian patients suffering from amoebic dysentery, 7 of whom had previously been treated with a variety of specific drugs (including emetine and aureomycin), were treated with "Resotren". The dosage was one tablet ($\frac{1}{2}$ gm.) of the drug thrice daily for the first day ; 2 tablets thrice daily from the second to the seventh day ; and then one tablet thrice daily from the eighth to the fourteenth day ; a total of 60 tablets, or 30 gm. of the compound.

The abdominal symptoms and diarrhoea in all cases cleared by the end of the first week ; the stools became free from parasites in 14 of the cases by the sixth day, but parasites persisted in the stools of one patient. The amoebic hepatitis evident in one of the patients apparently vanished during treatment, but as the patient absconded there was no follow-up in this case.

There were no side-effects of the drug except for slight diarrhoea lasting a couple of days. A. R. D. Adams

SCHNEIDER, J. & DUPOUX, R. Premiers essais de traitement de l'amibiase intestinale par l'acide p. sulfamido-o-amino-phénylarsinique. [**First Trials of Treatment of Intestinal Amoebiasis with p. sulphamido-o-amino-phenylarsinic Acid (1218F)**] *Bull. Soc. Path. Exot.* 1951, v. 44, Nos. 11/12, 741-3.

A compound prepared by Trefouël and described as "l'acide p-sulfamido-o-amino-phénylarsinique (1218F)" was found to be therapeutically effective in safe dosage in experimental amoebiasis in the rat. It was therefore considered suitable for therapeutic trial on human cases of amoebiasis. This paper is a preliminary report of the first trials.

Fifty patients, 11 of whom had previously been treated unsuccessfully with other amoebicides, were treated with this drug. The immediate result was amelioration of the clinical signs and disappearance of parasites from the stools by the 4th or 5th day of treatment. None of the 10 patients who were observed for 1 month to 4 months subsequently relapsed either clinically or parasitologically. The dosage given during the treatment of these individuals was at least 30 gm.; the impression was gained that a dosage of 20 gm. or less was inadequate, as when only 3 to 4 gm. were given daily for 5 to 7 days there was early parasitic relapse. The doses tentatively advocated for effective treatment are 4 to 5 gm. daily for 8 to 10 consecutive days. No significant toxic side-effects resulted from the administration of the drug to a total dosage greater than this. It therefore seems to be an extremely well tolerated and effective amoebicide, as far as the preliminary investigations show.

A. R. D. Adams

CHATTERJEE, P. K. & ROY, B. B. **Aureomycin in Amoebiasis.** *J. Indian Med. Ass.* 1952, Feb., v. 21, No. 5, 215-16.

"(1) A case of liver abscess bursting into the peritoneum is described in which aureomycin treatment had no effect on the amoebic process.

"(2) A case of infective hepatitis has been described where during the course of aureomycin treatment, an acute attack of amoebic dysentery developed."

PRESTON, P. J. **The Use of Aureomycin in Amoebiasis. A Report of Four Cases.** *J. Roy. Nav. Med. Serv.* 1951, v. 37, No. 3, 161-4.

KILLOUGH, J. H. **Aureomycin in Tropical Diseases with special reference to Amoebiasis and Brucellosis.** *Proc. Roy. Soc. Med.* 1952, Mar., v. 45, No. 3, 109-12 (Sect. Exper. Med. & Therap. 9-12), 1 fig.

HUTTEL, W. Traitement de l'amibiase par la terramycine. [**Treatment of Amoebiasis with Terramycin**] *Bull. Soc. Path. Exot.* 1951, v. 44, Nos. 11/12, 744-7.

Some patients suffering from amoebiasis were treated with terramycin in the Gabon (A.E.F.). Examples are given of the treatment of an acute case, of a chronic case, and of one suffering from both intestinal and hepatic amoebiasis. In each case the symptoms vanished within 48 hours of beginning treatment; and the stools became negative by at latest the fourth day. The enlargement of the liver of a third patient had subsided by the fourth day. The conclusion is reached that terramycin given orally at a dosage of 2 gm. daily for 10 days is therapeutically effective in all forms of amoebiasis.

In the discussion which followed SCHNEIDER said that terramycin, like aureomycin, produces a satisfactory immediate clinical and parasitological

response in intestinal amoebiasis. But this action is transitory, because clinical and parasitological relapse occurs ; 35 patients were treated by him with 2 gm. of the drug daily for 10 to 15 days ; in every case there was a parasitological, and often a clinical, relapse within a few weeks. Furthermore, terramycin is not always well tolerated, there being abdominal pain and sometimes diarrhoea ; in one case there was a morbilliform eruption. The action of terramycin on the disease is indirect, in that it appears to be on the accompanying bacterial flora rather than on the amoebae.

A. R. D. Adams

PRIETO LORENZO, A. & FERNÁNDEZ NAFRIA, A. Giardiasis. [*Giardiasis*] *Med. Colonial*. Madrid. 1952, Mar. 1, v. 19, No. 3, 216-42, 3 figs. [79 refs.]

A general review.

MCCAREY, A. G. **Balantidiasis in South Persia.** *Brit. Med. J.* 1952, Mar. 22, 629-31. [16 refs.]

Eighty-seven cases of balantidiasis have been diagnosed in S. Persia between April 1 and December 31, 1948. They all occurred among the inhabitants of Abadan, on the island situated in the estuary of the Shatt-el-Arab river, with a population of about 200,000 Persians, 2,000 Indians and Pakistanis and 5,000 British. All in this series were Mohammedans, therefore any contact with pigs can be excluded. No cysts were found in the stools and no source of infection, apart from human cases, was discovered.

Clinical features consisted of diarrhoea, abdominal pain, tenesmus and the passage of blood and mucus. In uncomplicated cases the symptoms were mild. Seven patients had concomitant bacillary dysentery and one amoebic dysentery. Small discrete ulcers were found in the lower bowel in 11, in scrapings of which numerous balantidia were found.

In treatment, sulphaguanidine, mepacrine and mercury biniodide were failures. *Acetarsol* (Stovarsol) was successful and is regarded as being very effective.

The drug was given to 81 persons. Eleven were given 4 grains thrice daily for five days, 50 were given the same dose till the stools became negative.

Twenty who were positive at the follow-up or had relapsed within 6 months were also treated till the stools became negative. Philip Manson-Bahr

LAMY, L. & LAMY, H. Déterminisme de la zygose chez *Balantidium coli*, en culture. Action de la température. [**Effect of Temperature on Conjugation of *Balantidium coli* in Culture**] *C.R. Soc. Biol.* 1951, July, v. 145, Nos. 13/14, 994-6, 1 fig.

When cultures of *Balantidium coli* are maintained at 37°C., they have to be subinoculated every 4 days. The authors have been able to prolong the period of survival of the ciliates by cultivating them at 25°C. in a fluid medium containing horse serum, saline and rice starch. Under these conditions subcultures were required only every 8-10 days.

It was observed that at 37°C. the ciliates conjugated regularly but when subcultures were maintained at 25°C. they ceased to conjugate after one month. In a non-conjugating culture maintained at 25°C. for over one year, unsuccessful attempts were made to induce conjugation by addition of various chemicals. But when such cultures were incubated at 37°C. the ciliates entered into a period of conjugation after 48 hours.

The effect of raising the temperature of the cultures upon conjugation was studied further by varying the period of time during which the cultures were kept at 25° before being transferred to 37°.

These observations indicated that conjugation was invariably induced under these conditions, but its intensity depended on the length of the previous period of maintenance at 25°. The optimum conditions for conjugation were during the first 48 hours after a culture, which had been kept at 25° for 1-3 days, was transferred to 37°.

In order to determine the time required to induce conjugation at 37°, cultures were kept at this temperature for 6 to 24 hours and then transferred to 25°. An examination of these cultures showed that a minimum period of 21 hours at 37° was required to induce conjugation: if they were exposed to the higher temperature for shorter periods, conjugation did not take place [see also this *Bulletin*, 1951, v. 48, 265].

C. A. Hoare

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

AGARWAL, B. L. **Relapsing Fever in Kashmir.** *Indian Med. Gaz.* 1951, Oct., v. 86, No. 10, 446-53, 5 figs. [16 refs.]

Tick-borne relapsing fever was first reported in Indian army troops in Kashmir in 1949. Until then relapsing fever was not known in this State, but it is possible that the disease was present but not recognized owing to its mildness and lack of mortality among the indigenous population [as in the case of certain districts in Central Africa].

This report is based on a study of 48 patients treated in a military hospital over a period of 10 months in 1949, the diagnosis in all cases being confirmed by blood examination.

The vector concerned in transmission was found to be a tick, *Ornithodoros crossi*, and not a louse. A table of the monthly admissions of cases of relapsing fever to military hospitals (163 cases) from Oct. 1948 to Oct. 1949 shows the highest figure (44) for Nov. 1948 and the lowest (3) for Sept. 1949.

Factors affecting incidence were considered to be :—

1. Movement of troops constantly on the move, who may have to stay in tick-infested huts.

2. Insecticides used regularly (*e.g.*, DDT) will considerably reduce the number of ticks in buildings, and thus stationary troops in barracks which are regularly sprayed showed a very low incidence. Decreased admissions from Jan. 1949 may be explained by the establishment of "Cease Fire" and the resulting diminution in troop movements.

Clinically the first and usually chief manifestation of the illness was fever, ushered in by a severe chill or rigor, and usually accompanied by headache. Sixty-three per cent. of patients complained of persistent giddiness, while cough and signs of bronchitis were common, also aches, pains in the back, weakness and prostration. Mental symptoms consisted of mild delirium, confusion, and slight disorientation. The spleen was palpable in 36 per cent. of cases and in half of these regressed after treatment. The liver was palpable and tender in 15 per cent. and in one case jaundice was observed. One patient showed a positive Kernig's sign, with very intense headache.

The maximum number of relapses seen was 11 over a period of 121 days, the initial pyrexia averaged 4½ days, the first relapse 2 and subsequent relapses 1 day. [No mention is made of eye complications so common in the Central African type.]

Forty-six of the 48 patients showed a positive blood film during one of the febrile attacks, diagnosis in the remaining two being made by rat inoculation. Sternal puncture during an apyrexial period was performed in 7 cases but with negative results. Twenty per cent. showed an excess of urobilinogen in the urine, which cleared after treatment. Wassermann and Kahn reactions were negative in the 16 cases in which these tests were performed. The blood sedimentation test gave no significant findings. Lumbar puncture done in one case showed cerebrospinal fluid under pressure with 160 cells per cmm. (mostly lymphocytes), but no spirochaetes.

In this series 26 patients were treated with NAB [neoarsphenamine] and 22 with streptomycin.

Doses of 0.45 and 0.6 gm. of NAB were given intravenously at an interval of 5 or 6 days, total 1.05 gm., but two patients received 2.25 and 2.1 gm. respectively. In the majority of cases it was considered unsafe to give the drug during pyrexia owing to fear of collapse [?]. Nine patients of 26 treated with NAB relapsed, none of these being among those who had had treatment during a febrile period.

Two injections of 0.5 gm. of streptomycin in normal saline were given intramuscularly each day for two days. One patient received two courses of 2 gm. each and another 3 gm. in three days. Nearly half the 22 patients treated with streptomycin showed a rise of temperature accompanied by an aggravation of symptoms, and 7 had a relapse after treatment.

It was concluded that both NAB and streptomycin were equally efficacious, but that the value of the latter drug lay in the treatment of those failing to respond to NAB or in cases where this drug may be contraindicated owing to renal or hepatic complications. It is suggested that streptomycin should be given a trial in the more severe louse-borne infections.

[This does not appear to be a very convincing paper as to relative efficacy of NAB and streptomycin. In the opinion of the abstracter the courses of NAB have been too short and the dangers of giving it, especially in small or moderate doses, unduly stressed.]

C. F. Shelton

ROLLO, I. M. & WILLIAMSON, J. **Acquired Resistance to Penicillin and to Neoarsphenamine in *Spirochaeta recurrentis*.** With a statistical addendum by R. L. PLACKETT. *Brit. J. Pharmacol. & Chemotherapy*. 1952, Mar., v. 7, No. 1, 33-41, 3 figs. [15 refs.]

"1. Two strains of *Spirochaeta recurrentis* (*S. duttoni*) have been passaged over a long period in a series of mice subjected to treatment with penicillin and with neoarsphenamine, respectively, in an attempt to demonstrate acquired drug resistance.

"2. After a period of three years, two and three-quarter months, involving 294 treated passages, acquired resistance to penicillin was observed, but the resistance was no more than twice that of the parent strain. After a period of two years eleven months, involving 295 treated passages, an approximately eightfold increase in neoarsphenamine resistance was observed.

"3. The assay procedure was based on an estimation of infection level by a differential parasite/erythrocyte count on heavily infected mice inoculated, treated, and examined under controlled conditions.

"4. The results have been subjected to statistical analysis for assessment of significance."

YAWS

AMPOFO, O. & FINDLAY, G. M. **Terramycin in the Treatment of Yaws and Tropical Ulcer.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1951, Oct., v. 45, No. 2, 261-3. [12 refs.]

The authors refer briefly to the treatment of yaws by means of the newer antibiotics, with particular reference to terramycin [see also this *Bulletin*, 1951, v. 48, 369, and above, p. 647]. They then describe the treatment of 6 patients, aged 4 to 12, in the Gold Coast, who suffered from secondary yaws.

Three patients received 2 gm. terramycin daily and the other three 1.5 gm. daily in divided doses by mouth continued for 7 days. There was no difference in the rate of healing in the two series. Pain disappeared in 24 hours and spirochaetes in 24-36 hours. Healing of the lesions was complete in 1 to 4 days and there has been no recurrence in the 3 months period of follow-up. In each case the Kahn reaction, originally positive, has shown a decrease, but there has been no complete reversion to negative.

One of the patients also had a tropical ulcer on the left leg. The yaws lesions healed in 36-48 hours and the tropical ulcer showed no organisms in smears after 48 hours, although there had been masses of fusiform bacilli and spirochaetes in the pus before treatment. The tropical ulcer had healed completely 14 days after treatment.

The authors therefore treated 5 more children with tropical ulcer. Each received 1.5 gm. of terramycin daily, in divided doses, for 7 days. Within 48 hours, there were no spirochaetes and only a few fusiform bacilli in the smears. In 72 hours the ulcers were sterile (3 had shown cocci in the smear as well as the characteristic flora). No relapse occurred during the 3 months of observation. There was no evidence of toxicity. The authors note that while "terramycin thus takes its place with aureomycin and chloramphenicol as one of the antibiotics which are active, when given by mouth, in the treatment both of yaws and tropical ulcer, two of the most widespread and disabling diseases of the tropics", it has the advantage of apparent complete absence of toxicity. The authors wisely observe that it is yet too early to determine which of these antibiotics is the most suitable for mass treatment [for work on chloramphenicol, see this *Bulletin*, 1951, v. 48, 1118].

H. J. O'D. Burke-Gaffney

LEPROSY

SOCIETY OF FRIENDS OF LEPERS. ACCRA. **They that Walk in Darkness. The Cure and Prevention of Leprosy in the Gold Coast (by a Doctor).** 23 pp., 6 figs. [1952] Accra : P.O. Box 778.

This pamphlet has been written in English by a doctor, and it is intended that it should be translated into the various vernaculars of the Gold Coast. In the introduction it says : " For more than a thousand years there has been Leprosy in our country : but we mean to change these things. We, in the Gold Coast, are not content to live in poverty and to die of disease. We plan for the great future of our country, when all the knowledge of Medicine and Science will be at the service of our people." The pamphlet itself takes the form of a series of questions which are answered in the simplest possible way, thus : What is Leprosy ? How does the Sickness Develop ? Are all Cases of Leprosy Dangerous to other People ? Can anyone catch Leprosy ? Is Leprosy Hereditary ? Can Leprosy be Cured ? How is Leprosy Treated ? and so on

to the last question : How are we trying to fight Leprosy in the Gold Coast ? The pamphlet is illustrated with a few photographs showing the different types of cases, and the effects of treatment. It is issued by a body called the *Society of Friends of Lepers*. As the Chairman of this society writes in a covering letter, "literature of this type is widely required in the tropics today".

Ernest Muir

RAGUSIN, E. La lèpre en Nouvelle-Calédonie et dépendances. [**Leprosy in New Caledonia and Dependencies**] *Internat. J. Leprosy*. New Orleans. 1951, Oct.-Dec., v. 19, No. 4, 413-21.

Leprosy is supposed to have existed in New Caledonia for a long time, but was confined to the east coast. It is supposed to have been the revolt of the indigenous inhabitants in 1878 that led to mixing with other tribes and generalization of the disease. In 1889 the first white case was notified, and by 1892 there were 37 known cases. The first precise statistics were those of LEBOEUF in 1911-12. He found 1,000 indigenous cases, about 4 per cent. of the population, and 154 cases among whites. The population of New Caledonia is 22,000 Europeans, 32,000 indigenous and 6,000 Asiatics. In 1950 the known persons with leprosy among these 3 communities totalled 1,075, of whom 140 were Europeans. The earlier methods of control attempted were severe and led to concealment, so that most of those affected had had the disease for several years before they were found. More humane measures are now being attempted. "Almost all of the noncontagious natives are living among their tribes. The 316 contagious cases are isolated."

Ernest Muir

WADE, H. W. **Demonstration of Acid-Fast Bacilli in Tissue Sections.** *Amer. J. Path.* 1952, Jan.-Feb., v. 28, No. 1, 157-70. [17 refs.]

This paper consists of two parts, the first dealing with paraffin section procedures, and the second with the new method of mounting tissues in carbowax. The procedure of preparation of paraffin sections tends to remove to a certain extent the acid-fastness of lepra bacilli. This is due to the use of two different reagents (say, cedar oil and xylene) at different stages in the process. The first of these "conditions" the bacilli in such a way that the second removes the acid-fastness. This difficulty can be got over in one or both of two ways, *protection* and *restoration*. The author's original method of protection was to use essential oils both for removing the paraffin and for clearing. For restoring acid-fastness after it has been once lost Fite's modification of Faraco's method is described. In this, paraffin is removed by the use of a mixture of 2 parts of xylene and one part of cotton-seed or similar oil, and the sections are then dried in the air before mounting. The oil retained in the section prevents shrinkage. The author's modification of Fite's method uses a 1 : 2 mixture of paraffin oil and high-test gasolene. This is found to be less damaging and more restorative of old or damaged bacilli ; alternatively turpentine replaces the gasolene in the mixture.

A more effective and easier procedure is to use carbowax in place of paraffin. This substance consists of a mixture of polyethylene glycols in which tissues can be embedded directly from water or alcohol. "They have proved entirely practicable, once the technician becomes accustomed to the characteristics of this odd medium." There are various grades, and a 2 : 8 mixture of the 1540 variety with the 4000 is best, with an alternative of a 15 : 85 mixture if the temperature reaches 90°F. As with paraffin sections, bacilli can be made to stain better in carbowax sections by restorative treatment, preferably by

soaking in the gasoline-oil mixture for 2 or 3 hours. Full details of all these techniques are given, for which the reader is referred to the original article.

Ernest Muir

FERRER, D. & RIBAS MUJAL, A. Neuromas de la placa motriz en la lepra. [**Neuromas of Motor Nerve-Endings in Leprosy**] *Rev. "Fontilles"*. Valencia. 1951, July, v. 2, No. 8, 607-11, 5 figs. [12 refs.]

The material examined was taken from the ala nasi, and when received by the authors had already been sectioned for a considerable time. It was taken from a case of lepromatous leprosy. Some of the motor nerve-endings, as shown in illustrations, have the form of globular dilatations or of varicose irregularities, and alongside of them are others of normal structure. The authors, by searching the literature, were able to find only one other similar description, that by LAWRENTJEW and FILATOVA described in tuberculous laryngitis. They question whether there is a common factor in the organisms of leprosy and tuberculosis which can produce this phenomenon.

Ernest Muir

ROSS, Hilary & GEMAR, F. **Studies on Serum Proteins in Leprosy. The Alpha, Beta and Gamma Globulin Fractions.** *Internat. J. Leprosy*. New Orleans. 1951, Oct.-Dec., v. 19, No. 4, 445-52, 3 figs.

The serum specimens of 234 leprosy cases of all types and stages of activity of the disease were examined in order to estimate total serum protein, albumin, total globulin, and alpha, beta and gamma globulin fractions. Specimens from 29 employees at Carville were used as controls. The findings were correlated with results from thymol turbidity tests and cephalin-cholesterol flocculation tests. Elevation of the serum globulin fractions occurred in over half the cases and was found most frequently in the moderately advanced and far advanced lepromatous cases. There was more regularly an increase in gamma globulin than in either the alpha or beta fractions.

Ernest Muir

ARCURI, F. & CANNATA, C. L'eliminazione giornaliera dei 17-chetosteroidi urinari nella lebbra. [**The Daily Excretion of Urinary 17-Ketosteroids in Leprosy**] *Acta Med. Italica*. 1952, Jan., v. 7, No. 1, 1-4. [28 refs.]

The English summary appended to the paper is as follows :—

"The authors have studied the daily elimination of the urinary 17 chetosteroids in 28 lepers, using, for the dosage, the Pincus-Salter and Zimmermann-Callow technics. They have found, in 68 per cent of the cases, noticeable variations, superior or inferior to the normal, of the excretory values of these substances. They did not notice a correlation between the excretion of the androgens and the type, extent and course of the disease.

"They point out some interpretative hypothesis about the results of their investigation."

POINDEXTER, H. A. **A Clinical and Laboratory Study of Leprosy in Liberia.** *Internat. J. Leprosy*. New Orleans. 1951, Oct.-Dec., v. 19, No. 4, 395-411. [12 refs.]

In the 2 million inhabitants of Liberia there are about 1,200 easily recognized cases of leprosy, a prevalence rate of about 0.6 per cent. But it is estimated that there are probably 2,000 cases altogether. There are between 1,100 and 1,200 patients in the 4 leprosy colonies, and 180 others are treated as out-patients.

A detailed clinical and laboratory study was made at Ganta, one of these colonies belonging to the Methodist mission. Only 14 per cent. were lepromatous cases, but 39 per cent. of the maculo-anaesthetic cases were also found to be bacteriologically positive. Diasone was given to 12 bacteriologically positive patients for 9 months, and the results were compared with those under chaulmoogra treatment, the greater improvement being very striking. Details are given of the various complications, from which the patients suffer. "Observations indicate that leprosy reduces the procreative power of both sexes, more in the male than the female. Nodular leprosy causes twice as many unproductive marriages as the anesthetic type. It also appears that little more than 10 per cent. of the products of conception in patients over 30 years of age survive to adolescence."

Ernest Muir

GÓMEZ ORBANEJA, J. Lepra tuberculoide. [**Tuberculoïd Leprosy**] *Rev. "Fontilles"*. Valencia. 1951, July, v. 2, No. 8, 585-606, 14 figs. on 8 pls.

In this critical study of tuberculoïd leprosy the condition is sub-classified into typical and atypical leprides with a transitional category in between. Typical leprides are again divided into quiescent or torpid, and reacting. The quiescent form may take two forms: the sarcoid lepride with a raised margin and a flat depigmented centre, and the nodular or lupoid, the whole of which is raised. The author has not experienced much benefit from sulphone treatment, but the number of cases treated and the method of treatment are not mentioned. The article is illustrated with 5 photographs and 9 photomicrographs; it should be of value especially to Spanish doctors not acquainted with the condition.

Ernest Muir

LEPROSY REVIEW. 1952, Jan., v. 23, No. 1, 30-35. **Findings of a Meeting of Leprosy Workers concerning the Sulphone Treatment of Leprosy.**

The main object of this meeting of leprosy workers with experience, chiefly in India and Africa, was to come to agreements regarding the use of sulphones in leprosy, and issue statements for the guidance of workers in the field. Out of all the sulphones available the two chosen as most suitable were sulphetrone, given in a watery solution intramuscularly or subcutaneously, and DDS orally in tablet form. While both of these were considered effective there was a difference of opinion as to which of the two was the better, some advocating the former as being considered less toxic and the others preferring the latter as no more toxic in suitable doses, and as being cheaper and easier to administer. It was agreed that in using DDS tablets certain precautions should be taken, the patient not being given tablets to take away with him unless the physician could trust him to use them according to instructions. The complications of sulphone treatment were discussed, but most of these were considered to be the results of excessive dosage. Sulphetrone should be injected twice a week, beginning with 0.5 cc. of a 50 per cent. watery solution, and increasing the dose every fortnight by 0.5 cc. till 3.0 cc. twice a week is reached. DDS, given orally, should begin with 100 mgm. twice a week, the dose being increased by 100 mgm. every month up to a maximum of 400 mgm. twice a week. The length of treatment should vary with the severity of the case and the time taken to become negative, periodic courses of after-treatment being considered where practicable. It was emphasized that sulphone treatment alone is not the answer to the wide problems of leprosy. Early diagnosis, the early institution of treatment, segregation of infective cases, other remedial measures including surgery, all these activities are vital.

The use of other drugs such as streptomycin and thiosemicarbazones were discussed and their value recognized as auxiliaries or alternatives. The results obtained with BCG in rendering the reaction to lepromin antigen positive, was discussed, especially the work done recently in Brazil [see this *Bulletin*, 1951, v. 48, 1121]. It was agreed that if these findings are confirmed, and if BCG is found to increase the resistance of children to leprosy, we may have another important tool in combating the disease. *Ernest Muir*

LOWE, J. **Studies in Sulphone Therapy.** *Leprosy Review*. 1952, Jan., v. 23, No. 1, 4-29. [36 refs.]

This comprehensive paper is divided into two parts: "The Mode and Action of Sulphones", and "The Use of DADPS" [or DDS as is the more usual symbol]. Several papers on this subject have already been published by the author [this *Bulletin*, 1951, v. 48, 374, 649, 1000, 1124]; the object of the present paper is "to summarize the available published information, and to present the results of our further investigations". After summarizing the work of British, French and Brazilian workers, all of whom are increasingly using DADPS in place of the more complicated disubstituted sulphones, he writes: "It has been found that small doses of DADPS are safe and well tolerated, and give the full therapeutic effect in treatment". WADE is quoted as saying "a widely accepted doctrine of sulphone activity demands, besides the *para* relationship of the essential constituent groups, that one or both amino groups be free or potentially free. Theoretically, because in promin, diasone and sulphetrone both the amino groups are occupied by substituents, they should be "blocked" and hence inactive". Wade goes on to say that *because of their instability* this is not so in practice.

The author then describes the methods used in distinguishing between DADPS and the disubstituted derivatives as found in the blood, urine, etc. This depends largely on the fact that DADPS is readily soluble in organic solvents, but practically insoluble in water, while the disubstituted sulphones are readily soluble in water but insoluble in organic solvents. Oral administration of the three disubstituted sulphones produced, according to the dose, various total sulphone and various DADPS concentrations. These are given in tabular form. "Sulphetrone usually given by mouth in doses of 3-6 g a day, gives at these dosage levels a free DADPS blood level of 0.2 to 0.5 mg %. Diasone in its usual dose of 0.9 to 1.8 g a day gives a DADPS blood level from 0.2 to 0.6 mg %. Promin has rarely been given by mouth as it is considered too toxic; we have found the tolerated dose is not more than 0.8 g a day, and this we find gives a DADPS blood level of about 0.8 mg %.

"It will also be noted that the usual dose of these sulphones, which has been based on the tolerated dose, varies inversely with the degree to which the particular sulphone produces DADPS in the body."

The author goes on to say that evidence is strong that the therapeutic blood level of DADPS is certainly as low as 0.2 mgm. per cent., and that this level of DADPS concentration is attained and often much exceeded when the complex sulphones are given in their usual doses. It therefore appears unnecessary to postulate any additional action of the undegraded complex sulphone. With regard to the injection of disubstituted sulphones, there is evidence that very little DADPS is produced in the body after such injections. If their therapeutic activity is due entirely to DADPS the therapeutic activity of DADPS is very low. "On the other hand it is possible that injections of disubstituted sulphones are therapeutically active, partly because in the solutions before injection, or in the body after injection, mono-substituted sulphones are produced, and these are active."

In the second half of the paper the author considers the maximum tolerated dose, the minimum therapeutic dose, and the optimum therapeutic dose. Regarding the first he concludes that the maximum well-tolerated dose is 200 mgm. per day, or 500 mgm. twice weekly. To ascertain the minimum therapeutic dose 6 previously untreated tuberculoid-type patients were given successively, for periods of 2 months each, 15 mgm. a day, then 30 mgm. a day, then 50 mgm. a day, and lastly 100 mgm. a day. During the period of 15 mgm. dosage 4 out of the 6 gave a slow but definite response to treatment. During the 30 mgm. period all 6 cases showed slow but definite progress, and this was more rapid during the 50 mgm. period. During the 100 mgm. period improvement was maintained but showed little acceleration if any. "The experiment was interpreted as indicating that doses as low as 30 mg a day, and blood levels as low as 0.2 mg % are capable of producing a clinical response in such cases, but probably not the maximum response." Regarding the optimum therapeutic dose, "more recent experience has shown that twice weekly treatment with doses rising slowly to 400 mg, is better tolerated than daily treatment with 200 mg. a day, the complications being fewer and less severe and interruptions in treatment being fewer. Possibly for this reason, the response to treatment appears to be at least as good as, if not better than, that seen with 200 mg a day." Twice weekly treatment with 400 mgm. produces a maximum concentration of about 0.8 mgm. per cent. which falls to about 0.3 mgm. per cent. before the next dose. On 500 mgm. once-weekly doses the maximum is a little higher and the minimum a little lower. If intramuscular injections are used, the maxima are lower and the minima are higher. "Our experience here indicates that the optimum dosage for good tolerance and good therapeutic response is a dosage rising slowly to 400 mg twice a week, though it appears possible, if not probable, that 200-300 mg given twice weekly, or the 400-500 mg given once a week would give equally good results."

Next is an interesting section on absorption, metabolism, storage, excretion and toxicity. Absorption is almost complete, and about 85 per cent. of the sulphone given appears later in the urine. Absorption is very rapid; DHARMENDRA'S report is confirmed that after administration of a single dose sulphone appears in the blood within 10 minutes. When the blood of a patient getting DADPS is examined, about 80 per cent. is found as free DADPS and 20 per cent. as water-soluble derivative. When the urine is examined "80 % of the sulphone excreted is no longer in the form of free DADPS, but is in a water-soluble form, presumably the same form which is found in much smaller amount in the circulating blood". It is the complete absorption and slow elimination of DADPS that makes it such an economic therapeutic agent and at the same time renders high doses dangerous. Acute toxicity is seen at blood levels of 2.0 mgm. per cent., for which administration of 2,000 mgm. a week is required. A safe blood level lies between 0.2 and 1.0 mgm. per cent. There is thus a considerable margin between the toxic and the therapeutic doses, the latter ranging between 300 and 1,200 mgm. per week.

The paper ends with *Sundry observations*. DADPS can be given safely to pregnant and nursing women, but in the latter a dose smaller than the usual one should be given in the first few weeks. Such treatment appears to avert the exacerbations so common during the puerperium, and may be of value in preventing leprosy infection by the mother in those cases where for any reason the child cannot be separated from the mother. Such Gram-positive infections as those by the pneumococcus, streptococcus and meningococcus are uncommon during DADPS treatment and may possibly be suppressed by DADPS, but Gram-negative infections are common. In tuberculosis the effect of DADPS alone is not marked, but "used in combination with streptomycin it appears to

have a definite action in preventing or delaying the appearance of streptomycin resistance".

[This paper is particularly worthy of careful study in the original, as want of space makes it necessary to omit from the abstract many items of interest.]

Ernest Muir

HERRERA, G. Tratamiento de la lepra con Propiosulfona. [**Treatment of Leprosy with Propiosulphone**] *Internat. J. Leprosy*. New Orleans. 1951, Oct.-Dec., v. 19, No. 4, 423-36, 12 figs. on 2 pls. English summary.

This is a water-soluble monosubstituted sulphone. When it is given by mouth, absorption is rapid and the drug reaches within the first 4 to 7 hours a concentration in the blood greater than that with sulphadiazine or sulphathiazole. But elimination is also rapid, and about 93 per cent. is excreted in the urine in the first 24 hours. Twelve leprosy patients were treated for periods of 9 to 15 months. These were in 3 groups. The first group comprised 7 patients, 3 of whom were reacting tuberculoids and 4 lepromatous, who had had no previous treatment. In the second group there were 3 lepromatous and one torpid tuberculoid case. In the third group there was a reacting tuberculoid. The initial dose was 1 gm. per day, and the maximum 3 gm. Seven of the patients showed total improvement within 15 months, 3 were markedly improved, and 2 moderately so. There were no febrile reactions and tolerance was good. The author concludes that the excellent efficiency of Propiosulphone in infectious leprosy, and the other desirable properties which it shows itself to possess, place it in a position of preference in sulphone treatment.

Ernest Muir

GATÉ, J. Essais de traitement de la lèpre par un dérivé hydrochaulmoogroyle de la D.D.S. Ses avantages au double point de vue de la tolérance et de l'activité lépridique. [**Trial of Leprosy Treatment with a Chaulmoogra Derivative of DDS**] *Bull. Acad. Nat. Méd.* 1952, v. 136, Nos. 1/2, 8-10.

This is a disubstituted derivative combining the fatty acids of chaulmoogra oil with DDS. This is injected intramuscularly in a 5 per cent. solu-suspension in chaulmoogra fatty acids. This preparation has been used with success in the treatment of 17 patients in the leprosarium at Lyons, and is found to be better tolerated by the patients than is DDS by mouth. Ulcers and nerve lesions heal up quickly, and there is less eye trouble than with the other forms of administration of the sulphones. Two injections of 10 cc. of the preparation are given up to 20 injections, after which there is a rest for 15 days.

Ernest Muir

KEIL, E. **The Treatment of Leprosy with Conteben.** *Internat. J. Leprosy*. New Orleans. 1951, Oct.-Dec., v. 19, No. 4, 437-44. [15 refs.]

Because of the resemblance of the aetiological agencies of tuberculosis and leprosy and the clinical characteristics which they both possess, it is logical to consider that any drug which is useful in the one disease might also be useful in the other. The thiosemicarbazone of Domagk, called "Conteben" in Germany, which is of proved value in tuberculosis, has given promising results in the treatment of leprosy. The author does not report any work of his own, but reviews the work of others who have used Conteben in tuberculosis and in leprosy, and compares the relative values of Conteben and sulphones in leprosy. He mentions allergic symptoms reported as being suffered by patients who had eaten salted fish during Conteben treatment, which symptoms can be weakened or suppressed by antihistamines. The author is of the opinion

that Conteben gives beneficial results more rapidly than sulphones and is better tolerated. Not only is it bacteriostatic but it acts as an anti-allergic agent, although under certain circumstances it itself causes allergy. Its main disadvantage is its higher price. It is necessary to use the optimum (25 to 50, rising to 100 mgm. a day) and not the maximum dosage.

Ernest Muir

LOWE, J. **Para-Acetamidobenzaldehyde Thiosemicarbazone in the Treatment of Leprosy.** *Lancet*. 1952, Mar. 1, 436-9.

This is a report of the results of treatment with this drug of 71 cases of leprosy over periods varying from 5 to 13 months, and averaging $8\frac{1}{2}$ months. The cases fall into three groups: Group A consisting of 30 of the lepromatous type previously untreated; Group B of 28 of the tuberculoid type previously untreated; and Group C of 13 lepromatous cases previously treated with sulphone, but difficult to treat because of complications. The product used was "Berculon A" supplied by Imperial Chemical (Pharmaceuticals) Ltd. The method of administration was to use 50 mgm. tablets, 1 tablet daily for 3 or 4 days, then 2 tablets daily for 3 or 4 days, then 3 tablets daily, one being given in the morning and two in the evening. Of the 71 patients only one suffered from serious toxic effects, developing agranulocytosis from which, however, he recovered quickly under penicillin treatment. In the other 70 patients there were only minor toxic effects. In Group A there was clinical improvement in all and bacteriological improvement in 21. In Group B, with tuberculoid cases mostly highly active, clinical activity slowly subsided and the patches became flat and residual within 6 months. In Group C there was clinical response to treatment in 12 of the 13 cases, though there was bacteriological improvement in only 5, "probably because the previous sulphone treatment had reduced the number of bacilli, and the later phases of bacteriological improvement under treatment are always slow".

According to the author, treatment of leprosy with this drug gives results similar to those with DDS. Allergy, shown by drug fever and dermatitis, has been much rarer and much milder with TB1 (thiosemicarbazone): complications of treatment have been fewer and milder than with DDS. Against this the author says "It is much less simple to give, however, and is more expensive. At present its use should be confined to selected inpatients of leprosy institutions, patients in whom the maintenance of sulphone treatment presents difficulties. It seems to be much less widely practicable than sulphone treatment, though it has certain definite advantages."

Ernest Muir

DRICOT, C. La thérapeutique moderne de la lèpre appliquée à un essai d'éradication de cette affection dans une région du Congo Belge. [**Modern Therapeutics of Leprosy Applied in an Attempt to Eradicate the Disease from a Region of the Belgian Congo**] *Bruxelles-Méd.* 1952, Mar. 2, v. 32, No. 9, 452-6.

The introduction of DDS has made it possible to reorganize the campaign against leprosy on new and more hopeful lines, with the prospect of bringing the disease under control. Patients will be divided into lepromatous who will be exclusively treated in leprosaria, and tuberculoid and other non-infectious patients who will be treated at home. The former will be given DDS by mouth, but the latter will be given DDS once a week or once a fortnight in the form of injections of a suspension in oil or esters. It is hoped that within 3 years about 50 per cent. of the lepromatous patients will be in a fit state to return to their homes. The lepromatous cases form less than 10 per cent.

of the whole. For this campaign it will be necessary to make a complete survey and much care will have to be exercised in making the classification, in which the Mitsuda test will have an important place. The removal of all but the lepromatous cases from the leprosaria will make it possible to give more attention to patients of that type, both as regards treatment and diet, and thus hasten their recovery.

Ernest Muir

HELMINTHIASIS

BERGSTERMANN, Heinrich, *et al.*, **Die parasitischen Würmer des Menschen in Europa. Ihre Biologie, Pathologie und Therapie.** [The Parasitic Worms of Man in Europe, their Biology, Pathology and Therapeutic Aspects]

This book was reviewed on p. 568.

VERNA, F. Le parassitosi intestinali nel territorio del Comune di Vicenza. [**Intestinal Parasites in the Town of Varese**] *Acta Med. Italica*. 1952, Jan., v. 7, No. 1, 5-10, 1 map. [12 refs.] English summary.

Varese, a town in Northern Italy, is situated close to the Alps and has a population of 60,000. The authors have studied the faeces of 1,082 pupils in 20 local schools and found *Ascaris* eggs in 178 and *Trichuris* in 156, giving an index of 28 per cent. for infestation with these 2 parasites. They found only one of 400 samples of soil collected from selected sites, often close to latrines, to show helminth eggs, 30 *Ascaris* eggs per field under the microscope. They have considered the findings in relation to the social and environmental conditions of the households from which the pupils came to the various schools and they have found that certain factors favour the higher incidence of these helminths, namely, overcrowded insanitary housing, prevalence of peasants and kitchen gardeners and lack of main water and of sewage. [In the title, the town is described as Vicenza, apparently in error.]

J. Cauchi

HUNTER, G. W., RITCHIE, L. S., KAUFMAN, E. H., PAN, C., YOKOGAWA, M., ISHII, N. & SZEWCZAK, J. T., with the technical assistance of R. E. WEBER, S. ASAKURA, Y. HISHINUMA & F. WILLIAMS, Jr. **Parasitological Studies in the Far East. IV. An Epidemiologic Survey in Yamanashi Prefecture, Honshu, Japan.** *Japanese Med. J.* 1951, Apr., v. 4, No. 2, 113-24. [14 refs.]

"1. An epidemiologic survey of intestinal parasites was made in the population centers of Kissawa, Kofu City, Otsuka, Hikawa, Sancho and Futakawa in the Kofu valley area of Yamanashi Prefecture.

"2. A total of 99.5% of the 3055 people who were examined harbored intestinal parasites; 99.4% were infected with helminths and 53.9% with protozoa. The incidence of the individual parasites is summarized in Table 1.

"3. Whipworm was encountered more frequently than ascaris, 91.6% and 88.8% respectively.

"4. On the basis of incidence data there did not appear to be any correlation between the occurrence of hookworm and the various agricultural pursuits, such as the raising of rice, mulberries or grapes.

"5. *Schistosoma japonicum* was found in about 65% of the individuals examined in two population centers, in about 30% of two others, and less than 5% in the remaining two. By multiple examinations an incidence of over 90% was shown to occur for children 11-15 years of age in several villages other than those included in the survey.

"6. *Endamoeba histolytica* was present in 10.3% of those examined, with a peak of 15.8% in one rural village. The lowest incidence occurred in two communities on the valley floor, while the highest occurred in hill-side villages.

"7. Helminth infections appeared to be of moderate intensity, but a large majority of the people harbored 3 to 5 different species. Probably 10% had severe ascariis, and 1% severe hookworm disease."

FAIRLEY, N. H. **Schistosomiasis and some of its Problems.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1951, Dec., v. 45, No. 3, 279-303. [Refs. pp. 304-6]

In this, his Presidential address to the Royal Society of Tropical Medicine and Hygiene, the author reviews the growth of our knowledge of schistosomiasis during and since the First World War. Throughout the whole of this period he himself has been a prominent and active contributor to this growth; an aspect of the matter, it may be added, which is not stressed in this paper. The paper contains many references to the vast literature and is in itself a most up-to-date summary of the subject; and so it does not lend itself to further condensation. Nevertheless a few points of particular interest may be selected for mention here. The successful specific treatment of schistosomiasis was originated by British workers in the Middle East during the First World War [this *Bulletin*, 1919, v. 13, 205, 206]. In spite of a national campaign against the disease in Egypt during the last 25 years, by treatment of those affected and by measures to control the snail vectors, there has so far been no material reduction in the incidence of the disease in the Nile Delta.

An antigen prepared from *Schistosoma spindale* has so far proved to be that most satisfactory for the performance of the complement deviation test on the sera of those infested with the human schistosomes. It is superior to an antigen prepared from *S. mansoni*. Infections of man with the cattle schistosome probably come to an end spontaneously; there is no evidence that *S. spindale* ever develops into the adult worm stage in man. There is much doubt as to whether man is truly susceptible to infection with *S. bovis* or *S. matthei*. It is possible, though improbable, that *S. intercalatum* is a strain of *S. matthei* locally adapted to man. Ectopic localization in the central nervous system of the ova of the human schistosomes when diffuse and scanty is probably due to embolism; the ova gain entry to the pulmonary veins and left heart through arterio-venous anastomoses in the lung; there are similar arterio-venous anastomoses in the liver. It is by this means that it is possible for ova to travel from the portal system to the lung, and then to pass into the systemic circulation.

These are but a few of the many facets of schistosomiasis touched upon by the author, which afford a lively stimulus to further investigation of the many so far unsolved problems of this fascinating disease. The paper is a mine of factual information, and it most certainly should be consulted in the original by all those interested in the subject.

A. R. D. Adams

COUTINHO, J. O. Contribuição ao estudo da esquistossomose mansônica no Estado da Bahia—Brasil. [**Schistosomiasis mansoni in the State of Bahia**] *Arquivos de Hig. e Saúde Pública.* S. Paulo. 1951, Mar., v. 16, No. 47, 3-42, 2 maps & 16 figs. on 6 pls. [Numerous refs.] English summary.

This work was awarded, by the São Paulo Medical Association, the prize for the best work on parasitology in 1950. It covers much more than the title would indicate, for the author quotes records for the past 25 years on the prevalence of *Schistosoma mansoni* infection not only in Bahia but in all Brazilian States. This is followed by a more intensive account of the infection

in Bahia itself, starting with a history and recordings from 1908 to 1950. The author finally gives an account of his own investigations. Laboratory diagnosis comprised examination of faeces for ova, rectal biopsy (only if other methods failed) and specific biological reactions such as the intradermo-reaction and fixation of complement; also study of Planorbid intermediate hosts. The incidence is calculated on a relatively small number of inhabitants examined, but the author comes to the conclusion that the infestation occurs all over the State. Among those examined by him the proportions were very high. Thus, of 500 patients in hospital just on half (49.8 per cent.) were infested and of 770 specimens of faeces examined 414, or 53.7 per cent. The 770 were made up of 279 in the capital itself, of which 138 (49.4 per cent.) were positive, and 491 in the interior, of which 276 (56.2) were positive. Again, of 321 men ready for military service and between 18 and 20 years of age, 173 (53.9) were positive, 92 out of 183 (50.2) from the capital and 81 of 138 (58.6) from the interior. The proportion appeared to be fairly general, for in another table is given the result of examination of 1,598 faecal specimens, 968 from males and 630 from females; of the former 545 (56.3 per cent.) and of the latter 293 (47.3) were positive. All races are affected: 410 of 844 whites (49.7); 267 of 478 mulattos (55.8) and 163 of 273 blacks (59.7). By allergic tests a still higher percentage of positives (63.4) was obtained. From 50 to 60 per cent. (730 among 1,325) of those between the ages of 10 and 40 years were passing the ova. The vectors are *Australorbis glabratus* and *A. olivaceus*. In Salvador, 20,881 snails were examined and 3 per cent. were found infected. *Tropicorbis centimetralis* is also found.

H. Harold Scott

GIRGIS, B. & MAGID, A. **Treatment of Schistosomiasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1952, Jan., v. 46, No. 1, 81-4.

GIRGIS and AZIZ [this *Bulletin*, 1948, v. 45, 446] have already reported on the intensive treatment of schistosomiasis, broadly following the method of ALVES and BLAIR [*ibid.*, 1946, v. 43, 344] with minor modifications. This paper is a report of further attempts to determine the optimum dosage of sodium antimonyl tartrate and the period over which treatment with it should be continued to ensure the highest percentage of cures with reasonable safety to the patient.

Forty Egyptian males suffering from uncomplicated schistosomiasis were treated with varying doses of sodium antimonyl tartrate as follows: in the first 8 cases the gross dosage was 18 mgm. per kgm. of body weight, which was divided into 6 equal injections given intravenously on the mornings of 6 successive days; in 4 cases the total was 24 mgm. per kgm., divided into 10 injections over 10 days; and in 28 cases it was 15 mgm. per kgm. divided into 6 doses over 6 days.

The patients given 18 and 24 mgm. per kgm. respectively suffered severe toxic reactions from the drug, and about a quarter of them had parasitic relapses. Those given 15 mgm. per kgm. suffered a minimum of toxic side-effects; 19 of these 28 patients had ceased to pass dead ova in the urine by the end of the third week but the other 9 continued to do so a month after the completion of treatment. Successful treatment [implying cure] is assumed when a patient ceases to pass both living and dead ova by the end of the third week after the last injection; the passage of even dead eggs after this date is regarded as a relapse. By these criteria, 67.8 per cent. of the 28 patients treated with 15 mgm. per kgm., divided into 6 portions daily over 6 days, were cured. (Three of the patients so cured had previously been treated and were passing only dead eggs in the urine at the time of commencement of this treatment.)

Taking into consideration the results previously obtained by treatment with 12 mgm. of sodium antimonyl tartrate per kgm. which are recorded in the paper already referred to, the authors conclude that for the intensive treatment of schistosomiasis the optimum dosage of sodium antimonyl tartrate lies between 12 and 15 mgm. per kgm. of body weight given in 6 injections over 6 days.

A. R. D. Adams

PRÉVOT, R., HORNBOSTEL, H. & DÖRKEN, H. Lokalisationsstudien bei *Taenia saginata*. [Studies on the Localization of *Taenia saginata*] *Klin. Woch.* 1952, Jan. 15, v. 30, Nos. 3/4, 78-80, 3 figs. [15 refs.]

The authors have studied the localization of *Taenia saginata* in the intestine by means of methods used for the X-ray demonstration of *Ascaris*. References are given to Italian authors who have used this method.

The authors wished to make visible the segments near the head in order that they might be better able to apply an anthelmintic directly in the neighbourhood of the scolex. It was clear at the outset that the narrow part of the tapeworm near the neck could not be demonstrated, but they believe that they could make out segments about 20 cm. below the scolex.

By far the majority of the *Taenia* seen were in the upper small intestine, the first detectable segments being about 40-50 cm. behind the duodeno-jejunal flexure. In only 3 of the 53 examinations made did they find the *Taenia* lower down, but even these were still in the jejunum. The worms were by no means passive and motionless, but often lay in several loops side by side in the form of a sling, a feature possibly due to movements of the worm directed against the peristaltic movements of the intestine. Various difficulties of the examinations are discussed and photographs show the appearances of the tapeworms.

The authors discuss von BONSDORFF's method of studying the localization of *Diphyllobothrium latum* by aspiration of its eggs by means of a duodenal sound. von Bonsdorff ascribed anaemia due to this tapeworm to a high localization of it in the intestine and thought that, when it is lower down, no anaemia is produced [this *Bulletin*, 1948, v. 45, 198, 260]. This changeable localization of *D. latum* contrasts with the constant position of *T. saginata* and is not readily explicable; but the authors adduce two criticisms of the method of investigation by aspiration of the eggs by means of a duodenal sound. First, the loops they demonstrated by the X-ray method, which, they suggest, can hardly fail to occur along the greater length of *D. latum*, can be misleading when eggs are aspirated above the point of attachment; and second, the length of the sound in the intestine measured from the patient's teeth seems to be an inaccurate estimate of the part of the intestine reached by the end of the sound. The sound does not always take the shortest route. X-ray examination showed, for instance, that the sound might form a loop in the stomach. The authors were unable to study patients infected with *D. latum*. Their treatment of *T. saginata* with atebirin [mepacrine] will be reported elsewhere.

G. Lapage

DE SA, A. E. & KOTHARE, S. N. Generalised Cysticercosis. A Case Report. *Indian J. Med. Sci.* 1952, Jan., v. 6, No. 1, 78-81, 2 figs. on pl.

NOR EL-DIN, G. Recent Advances in the Treatment of Intestinal Parasites. *J. Roy. Egyptian Med. Ass.* 1951, v. 34, No. 7, 449-61. [13 refs.]

Taeniasis.—The author treated 26 patients with atebirin [mepacrine]; he gave 8 to 10 tablets of atebirin in the morning on an empty stomach to adults

and followed this with a purgative—saline and castor oil. After one course of treatment 10 patients passed worms, after the second course 5 others passed worms and after a third course one more passed them. "Thus . . . a cure of 50 per cent was attained." [We make it 61·5 per cent.] Later, vomiting occurred in 3 cases and an urticarial rash in one.

Chloroquine was used in 51 cases; similar doses were given but in only 18 cases (35 per cent.) was the worm with its head passed.

With carbon tetrachloride worms were passed by 10 of 27 patients. Pumpkin seeds, an old household remedy, were used in 6 cases; the raw seeds and a decoction of seeds were given. Two patients who had resisted treatment by atebrin and male fern passed worms.

Hymenolepis.—For adults 10 tablets of atebrin were given on an empty stomach; children aged 10 to 15 years were given 6 to 8 tablets. This was followed by a follow-up course of 3 tablets daily for a week. Chloroquine was given in the same dosage [presumably] followed in half to one hour by a *small* dose of magnesium sulphate. The immediate result was "spectacular"; thousands of worms were found in the washed faeces. Of 25 patients treated with chloroquine 18 remained free of worms for 6 months. The results with atebrin were "as favourable".

Nausea and vomiting occurred in a few cases and these were attributed to too large doses of magnesium sulphate. Myasthenia occurred in one case.

Ascaris.—For this infection the author used hetrazan in doses of 3 to 4 tablets in the morning in one dose, repeated for 3 days at first. Children were given the same dose as adults. Later, he increased the dosage to 10 to 12 tablets daily for a week, for adults, and 6 to 8 tablets for children. No purgative was given as a routine. He had good results and considers it the drug of choice for this infection.

Enterobius.—Phenothiazine was given in doses of 4 gm. daily for 7 days for adults and 2 gm. for children. In 15 of 25 cases, a cure was obtained after the first course. No serious toxic symptoms occurred. The author also used certain *p*-benzyl-phenyl-carbamate drugs, such as diphenan, and anti-histamine drugs, such as benadryl, with success.

L. E. Napier

STUDER, A. & FUST, B. Durch parenterale Behandlung mit Askaridenextrakt ausgelöste Gewebs- und Bluteosinophilie beim Meerschweinchen und ihre Beeinflussung durch Cortison. [**Production of Eosinophilia in the Tissues and Blood of Guinea-pigs by Sensitization with *Ascaris* Extract and the Influence of Cortisone on the Eosinophilia**] *Ztschr. f. Hyg. u. Infektionskr.* 1951, Dec. 4, v. 133, No. 4, 327–43, 7 figs. (3 coloured). [31 refs.]

Studer and Fust sensitized guinea-pigs to extracts of *Ascaris* sp. and showed that cortisone reduces the eosinophilia in the blood, inhibits the tissue eosinophilia and lessens the clinical manifestation of shock on later exposure to *Ascaris* extract.

In the first experiment 20 guinea-pigs were sensitized by subcutaneous injections of 30 mgm. of an aqueous extract of *Ascaris* sp. on the first day and 60 mgm. on the 5th and 8th days. Ten of these were given cortisone by intramuscular injection 20 mgm./kgm. body weight twice daily on the 20th, 21st, 22nd, 23rd and 24th days, and 5 of these animals were given 65 mgm. of aqueous extract of *Ascaris* on the 25th, 26th and 27th days; on the 29th day some were killed and the sites of injection were examined histologically. Five others were exposed by inhalation to *Ascaris* antigen (10 minutes in an aerosol spray in a watery extract of 350 mgm./cc.) to provoke the symptoms of shock. Appropriate controls were used in each experiment. The tissue eosinophilia at the site of injection was lessened by cortisone, though the leucocytic and later round

cell reactions were uninfluenced. The clinical symptoms of shock in the animals exposed by inhalation—dyspnoea, shivering and apathy—were less marked in those animals which had had a previous course of cortisone injections.

In a second experiment designed to investigate the effect of cortisone on the blood eosinophilia, 10 animals were sensitized in a similar manner and cortisone was given in 10 mgm. doses twice a day each day throughout the experiment which lasted for 29 days, and 50 mgm. was given on the last day. Cortisone had little influence on the development of eosinophilia, but the eosinophilia caused by injections of the *Ascaris* extract on the 27th and 29th days was higher in the animals which had not had cortisone.

In a third experiment, the reduction in the blood eosinophilia was shown to be proportionate to the dosage of cortisone though there was a wide variability in the results.

In a fourth experiment, the duration of action of cortisone was investigated by taking 2 guineapigs which had a persistently high eosinophilia after sensitization, and giving injections of cortisone. The maximum fall in such animals occurred in 1–3 hours after the injection, and the eosinophile count returned to its original level within 2 days.

In an attempt to reproduce the experiments in rats with *Ascaris* extract, it was not found possible to evoke either the blood or the tissue eosinophilia by the methods used.

W. E. Kershaw

VAUGHN, J. **The Stimulation of the Eosinophil Leucocyte.** *J. Path. & Bact.* 1952, Jan., v. 64, No. 1, 91–102. [45 refs.]

“Extracts of *Ascaris suum* have been prepared and their potency in producing eosinophilia in normal unsensitized guinea-pigs demonstrated.

“One of these extracts (Ae. 2) has been shown to possess its eosinophilogenic power solely in respect of small amounts of the other extract (Ae. 1) adsorbed during the process of separation.

“In a limited examination of the chemical properties the intrinsically active extract has been found to be a mixture of polypeptides and other protein break-down products among which is to be found the active eosinophilogenic substance or its precursor.

“The effects of these extracts can be completely prevented by the administration of an anti-histamine drug.

“Histamine phosphate has been shown to have an eosinophilogenic activity resembling that of the extracts.

“Conclusions have been drawn in respect of the stimulus supplied to the bone marrow for the formation of eosinophil leucocytes.”

CASILE, M. & SACCHARIN, H. Sur un cas de lésions génitales lymphatico-veineuses dans la filariose de Bancroft. [**A Case of Filariasis (*W. bancrofti*) Showing Lymphatico-Venous Genital Lesions**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 1, 56–60. [15 refs.]

BASNUEVO, J. G., COWLEY, O., BLANCO RABASSA, E., ACHKAR, R. & MADURO, F. Cien casos de Tricocefaliasis curados con los enemas de Hexilresorcinol (Santokín). [**One Hundred Cases of Trichocephaliasis cured with Enemas of Hexylresorcinol (Santokín)**] *Rev. Kuba Med. Trop. y Parasit.* 1951, Sept.–Oct., v. 7, Nos. 9/10, 105–8. [10 refs.]

The English summary appended to the paper is as follows :—

“The authors refer to the use of enemas of Hexylresorcinol at 1 : 300 (Santokín Líquido) carried up the cecum in the treatment of Trichocephaliasis.

"They report 100% complete cures in 100 cases treated, from a clinical as well as parasitological point of view."

BASNUEVO, J. G., LAVÍN, F., BORBOLLA, Liane, RODRÍGUEZ SALINAS, E., COSTALES, F. & CEPERO, R. Nueve casos de Tricocefaliasis curados con los enemas de Hexylresorcinol (Santokín). [**Nine Cases of Trichocephaliasis cured with Enemas of Hexylresorcinol (Santokín)**] *Rev. Kuba Med. Trop. y Parasit.* 1951, Sept.-Oct., v. 7, Nos. 9/10, 119-27, 2 figs. [18 refs.]

The English summary appended to the paper is as follows:—

"The authors report 9 cases of Trichocephaliasis cured with enemas of Hexylresorcinol (Santokín Líquido) at 1 : 300, carried up to the cecum.

"The total volume of the enemas for children correspond, approximately, to 15 cc. per pound of body weight. They do not use over 1,200 or 1,500 cc. in adults weighing more than 80 pounds.

"The authors recommend the following formula for the enemas :

" Santokín (Hexylresorcinol 4 Gm.)	60 cc.
Acacia	120 Gm.
Kaolín	60 Gm.
Dried Aluminium Hydroxide Gel	60 Gm.
Water, s.q.f.	1,200 cc."

KLIMARS, G. Zur Pharmakologie einiger Oxyurenmittel. [**The Pharmacology of Substances used in the Treatment of Oxyuris Infestation**] *Ztschr. f. ärztl. Fortbildung.* 1952, Feb. 15, v. 46, Nos. 3/4, 91-5. [42 refs.]

This paper considers the chemical constitution and the vermifugal and possible toxic action of some of the newer medicaments used in the treatment of *Enterobius* infestations. Included among these are (1) hexylresorcin and other resorcinols and their derivatives, (2) a substituted carbaminic acid known as "Egressin" (Merck), (3) dye-stuffs such as malachite green, gentian violet and crystal violet, (4) the arthropod contact poisons—phenothiazine, DDT and benzene hexachloride, and (5) aluminium compounds.

High recommendation is given to the aluminium compounds because of their effectiveness and the complete absence during their use in treatment of toxicity or of unpleasant side-effects. The author uses a medicament called Oxymor, an insoluble aluminium compound (stated to consist of aluminium acetico-benzoicum) which is given internally, and also as an anal ointment (which also contains *p*-dichlorobenzene) and as an enema. M. E. Delafield

WELLS, Helen S., SHOOKHOFF, H. B., MULLIN, W. G., STERMAN, M. M., LOUGHLIN, E. H. & RAPPAORT, I. **Terramycin HC1 in the Treatment of Human Pinworm Infections.** *Antibiotics & Chemotherapy.* New York. 1951, Aug., v. 1, No. 5, 299-304.

One of the authors had already shown that terramycin had an adverse effect on the mouse pin-worm infection (*Aspicularis tetraptera*). LOUGHLIN *et al.* (in Press) reported uniformly successful treatment of *Enterobius vermicularis* infection with terramycin base, 2 gm. daily for 5 days, under institutional conditions.

An investigation was undertaken in the treatment with terramycin of *Enterobius vermicularis* infection in 61 persons living in their own homes. The diagnosis was established by Scotch [Cellophane] tape or NIH swabs. After treatment these swabs were taken by the clinic personnel or by a reliable

member of the patients' family after special training, as far as possible weekly up to 25 weeks after treatment. In most cases the whole families, infected and uninfected members, were treated and examined.

The treatment schedules for terramycin hydrochloride comprised an initial dosage four times daily for two days of 100 mgm. in children of 2-5 years, 250 mgm. in children 6 to 10 years and 500 mgm. in older children and adults, followed by doses of 50 mgm. four times daily, 250 mgm. twice daily and 250 mgm. four times daily, respectively, in the three age-groups, for two days, and maintenance doses 50 mgm., 250 mgm., and 250 mgm., daily respectively for 14 days.

The results were on the whole very satisfactory; however, the dose schedule is not considered ideal since there were several instances of apparent reinfection during maintenance dosage and in one instance treatment according to the schedule failed but a cure was effected with a slightly increased dosage.

The authors conclude that terramycin is more effective than gentian violet and is better tolerated, but that further investigations are needed to determine optimum dosage.

L. E. Napier

FRANK, J. F. **A Study of the Incidence of Trichinosis in Swine in the Maritime Provinces.** *Canadian J. Comp. Med.* 1952, Feb., v. 16, No. 2, 73-7. [12 refs.]

"Examination of diaphragms from 1,002 swine originating in the three Maritime provinces revealed the presence of trichinellid larvae in four diaphragms or 0.4 per cent. These were examined by both the compressorium and the digestion-Baermann techniques. All four positive samples were revealed by the digestion-Baermann technique while only three were revealed by the compressorium technique. The infected animals came from three different premises. On one of these, conditions were such that the complete life cycle of the parasite could be completed on the premises as raw offal from hogs slaughtered on the premises was being fed to the remaining swine. On the other two premises it was difficult to find the source of infection."

DEFICIENCY DISEASES

BENCHIMOL, A. B. & SCHLESINGER, P. **Coração beribérico. [The Heart in Beriberi]** *Med. Cirurg. Farmacia.* 1951, Nov., No. 187, 535-56, 12 figs. [45 refs.]

This was a paper presented at the World Congress on Cardiology, held at Paris in September, 1950. It comprises an analysis of 22 patients, all males, of ages ranging between 28 and 52 years, but most between 30 and 40 years. Oedema was the first sign in all but two. Only in 5 was ascites present and pleural effusion was also rare; dyspnoea was observed in all but two; hepatomegaly was present in all, polyneuritis in 20, but not in a severe form in any. The rest of the article is devoted to radiological changes, particularly the cardiac enlargements, to the electrocardiographic changes and tracings of numerous electrocardiograms, and the results of thiamine treatment on these. Six of the patients died and post-mortem examination was carried out on 5; the cardiac histology is depicted in two photomicrographs.

H. Harold Scott

SATO, A. & WAKO, H. **Methyl Glyoxal as Cause of Infantile Beriberi, Preliminary Report.** *Tohoku J. Exper. Med.* 1951, Dec. 25, v. 55, No. 1, 46.

ARAKAWA, T., WADA, S. & TAKAHASHI, F. **Nutritional Dystrophy with or without Macrocytic Anemia. Studies on the Nutrition of Children in Hirosaki Area. (9th Report.)** *Tohoku J. Exper. Med.* 1951, Dec. 25, v. 55, No. 1, 61-8, 1 fig.

"Nutritional dystrophy (infantile pellagra) is prevalent among children who visit us with other complaints in Hirosaki Area: We classified it into 3 forms:—'pellagrous form,' 'edematous form' and 'angular stomatitis form.'

"Macrocytic anemia seems to be more frequently found in both 'pellagrous' and 'edematous' forms than in 'angular stomatitis' form of nutritional dystrophy.

"Hyperchromic macrocytic anemia is found only in 'pellagrous form'."

HAEMATOLOGY

SHARMA & BHATIA, B. B. **Some Observations on Anaemia of Ancylostomiasis with special reference to Iron Therapy.** *Indian J. Med. Sci.* 1951, Sept., v. 5, No. 9, 454-60, 4 graphs.

"During the last 20 years, 762 cases of ancylostomiasis were admitted in the medical wards of K. G. Hospital, Lucknow." [It is not clear whether the patients were admitted as cases of ancylostomiasis or whether the infection was incidental.] The patients were 90 per cent. males [99.1 per cent. is the figure given in the table] and predominantly young adults; none was under 5 years of age.

The type of anaemia was ascertained in 135 cases; 80 per cent. were of the iron-deficiency type and the rest were normocytic or macrocytic.

The patients were treated [no details of the treatment are given, but the word "thymol" appears several times in the Figures] and the expelled worms were counted; these numbered from 1 to 200. A table of 52 cases shows no apparent relation between worm load and the red cell count and haemoglobin percentage; the most anaemic was 0.71 million red cells per cmm. and 6 per cent. haemoglobin.

When oral iron was given (Ferri et ammonii citras, 30 grains twice daily) the improvement in the blood position was only slight or absent, but after the patients were treated with anthelmintic there was a sharp rise in haemoglobin. A similar result was obtained with intravenous iron.

The authors conclude that the anaemia is due to some toxic substance elaborated by the worms which prevents utilization of iron.

[The paper contains no reference to other work on this subject. There is no statistical analysis of the authors' general results and their conclusions are apparently based on their findings in a very small number of cases: the Figures usually show curves of two or three individual cases only, and are thus obviously selected.]

L. E. Napier

PORTIER, A., MESSERSCHMITT, J. & MASSONNAT, J. **Fréquence et importance des syndromes hématologiques méditerranéens chez l'indigène musulman algérien. (Note préliminaire). [Frequency and Importance of the Mediterranean Anaemia. Syndrome in Algerian Moslems]** *Algérie Méd.* 1951, May, v. 55, No. 5, 899-906. [10 refs.]

BOTURÃO, Edmir. Sobre a drepanização dos eritrocitos de portadores e doentes. Método simples para a sua determinação. [**Sickle-Cell Subjects and Sicklaemia Patients. A Simple Method of Differentiation**] *Seara Méd.* S. Paulo. 1951, Oct.-Dec., v. 6, No. 4, 439-45, 7 figs. on pl. [17 refs.]

It has been known for some time that certain persons may have sickle cells in their blood picture without suffering from sickle-cell anaemia. The author has devised a method of distinguishing these two as extremes, but shows that intermediate grades may exist. His statements are based on a study of 32 subjects previously declared as sicklaemic by the Beck-Hertz standard.

The author's method is as follows: by means of a rubber band firmly applied the circulation of the terminal phalanx of the middle finger is stopped for 10 minutes; the finger is then pricked and applied to a slide on which is a drop of 10 per cent. formol, the finger being kept in contact to ensure mixing of the blood and the formol; the smear is then spread, stained and examined to determine the relative proportions of normal and deformed cells. Of the 32 examined it was determined that two were definitely cases of sickle-cell anaemia, the other 30 being merely sickle cell carriers, or with a tendency to sicklaemia, but without anaemia or any of the other symptoms which accompany this condition. One of the 32 was an intermediate case in which vague symptoms of excitability, convulsive crises, priapism and an anaemia which had been ascribed to helminthic infestation had been present, but had now cleared up. In a table the author divides his 32 cases as follows: 29 asymptomatic (8 with no deformed erythrocytes, 21 with 4.5 per cent. or less); one carrier with the 13.8 to 22.4 per cent. deformed cells (the intermediate case); one with "latent anaemia", 92.7 to 40 per cent., and one with active anaemia, 73 to 80 per cent. sickle cells.

H. Harold Scott

BOTURÃO, Edmir. Incidência da drepanocitose na Santa Casa de Santos. [**Incidence of Sicklaemia in Santa Casa de Santos**] *Seara Méd.* S. Paulo. 1951, Oct.-Dec., v. 6, No. 4, 447-9.

The author, with Edgar BOTURÃO, published the results of an investigation of 294 coloured persons and 64 whites in the Santa Casa Hospital, Rio de Janeiro, in 1947 [see this *Bulletin*, 1948, v. 45, 640]. None of the latter was affected but of the former 8.6 per cent. of the blacks and 4.5 per cent. of mulattoes were; the female percentage was greater than the male, 7.8 and 5.9 respectively [but see later]. The proportion of "sickle-cell carriers" to patients with sickle-cell disease was 7 to 1.

In 1951, another 337 patients in the hospital were studied by the Beck-Hertz technique and 8.6 per cent. showed sickle cells, 8.57 of the blacks and 8.61 of the mulattoes. Among those positive, males predominated, 9.58 per cent. to females 7.64 [according to the table, but in this table the 1947 figures are referred to and the sex-percentages as stated in the text, 7.8 females and 5.9 males are reversed]. The two totals amount together to 631 and 7.76 were positive, 8.88 per cent. mulattoes and 6.73 blacks. In the 1947 group the proportion was one with the disease to 7 carrier-positive; in the 1951 group none with the disease to 29 positive, with the two groups together 1 to 16.3. [In the table males are stated to make up 8.87 per cent. and females 6.8 per cent. of the total, but in the author's conclusions and summary these are reversed. Which is correct the abstracter cannot, of course, say, but in view of the fact that in one place it is stated quite definitely that women are in the majority, the mistake has probably occurred in copying out the table.]

For comparison 172 children of the Negro race, 6 to 14 years of age and apparently healthy, were examined; 5 had sickle cells (but not sicklaemia) 2.9 per cent., whereas of 25 children in hospital of the same age 3 were positive, recorded for comparison as 12 per cent. H. Harold Scott

JELLIFFE, D. B. **Cerebral Thrombosis in Sickle Cell Anaemia.** *West African Med. J.* 1952, Jan.-Feb.-Mar., v. 1 (n.s.), No. 1, 38-41, 4 figs.

VENOMS AND ANTIVENENES

TABORDA, A. R., TABORDA, Laura C., WILLIAMS, J. N., Jr. & ELVEHJEM, C. A. **A Study of the Ribonuclease Activity of Snake Venoms.** *J. Biol. Chem.* 1952, Jan., v. 194, No. 1, 227-33, 1 fig. [21 refs.]

"1. A study has been made of the ribonuclease activity of various snake venoms, particularly those of the genera *Bothrops* and *Crotalus*.

"2. The effects of various physical and chemical agents upon the ribonuclease activity of *Bothrops jararaca* venom have been studied in detail. The agents inhibiting the enzymes most markedly are heat, anti-Bothropic serum, formaldehyde, cysteine, cyanide, and cupric ions. The first four are agents known to be able to diminish or even completely neutralize the toxicity of snake venoms."

PRÉVOT, A. R. Recherches sur la pollution des venins de serpent par les anaérobies et leur stérilisation. [Study of the Contamination of Snake Venoms by Anaerobes and their Sterilization] *Ann. Inst. Pasteur.* 1951, Dec., v. 81, No. 6, 665-7.

Dried samples of various snake venoms were examined for viable bacteria. *Cerastes* and *Vipera aspis* venom were heavily infected with *Cl. welchii* type A and various cocci: *Bitis arietans* venom was only slightly infected; the only anaerobe isolated was *Cl. butyricum*. A very old sample of dried cobra venom was sterile. Samples of venom (0.01 gm./ml.) were readily sterilized by treatment with penicillin (1,000 units/ml.) for one hour, without effect on their toxicity.

The author ascribes the local lesions produced in horses by the injection of these venoms to the anaerobic organisms they contain. C. L. Oakley

FLECKER, H. **Fatal Stings to North Queensland Bathers.** *Med. J. Australia.* 1952, Jan. 12, v. 1, No. 2, 35-8.

[This is an interesting article which should do much to stimulate further research.] The author records several cases, mostly in children or young adults who, while bathing off the North Queensland coasts, have felt a sting and die in a very short time—a matter of minutes—with symptoms of anaphylactic shock, with sweating, collapse and cyanosis. Weals are found on the body, red or purple in colour, and frothy oedema of the lungs at autopsy, and little if anything more. Similar cases occurring in the Philippines, in Sydney and elsewhere have usually been ascribed to stings by the Medusa, *Physalia pelagica*, the Portuguese man-of-war, but in north Queensland at least this is not the only, and probably not the commonest, cause. The pearly dark-coloured float or bladder characteristic of *Physalia* is not seen and the cause is more probably *Chiropsalmus quadrigatus*, a member of the *Carybdeidae*: it is

known as the "sea wasp" and lives in large numbers in tropical and sub-tropical harbours and comes to the surface when mature. It has numerous tentacles with stinging cells. [There is room for fruitful study of the nature and mode of action of the virulent toxin it produces.]

H. Harold Scott

DERMATOLOGY AND FUNGUS DISEASES

COPLAND, W. A. **A Preliminary Survey of Skin Diseases in a Warship Commissioning in the Tropics.** *J. Roy. Nav. Med. Serv.* 1952, v. 38, No. 1, 8-15, 6 figs.

The incidence of prickly heat and toe rot (dermatophytosis of the feet) among the ship's complement (83 men) of an Algerine Class minesweeper increased by 25.3 and 36.1 per cent., respectively after one month in harbour and one month at sea in the tropics. Among the ratings, stokers and seamen showed the highest incidence of these skin diseases, and the average effective temperature of the living spaces of these groups (ca. 80°F.) was about 1.5°F. higher than that of the living spaces of the remaining ratings.

Surprisingly, the incidence of both skin conditions was higher in officers than any of the ratings, despite their better living conditions: effective temperatures of their living spaces are not, however, recorded.

The percentage incidence of prickly heat was lower among men who slept on deck than among those sleeping in their messes, but the reverse was true of toe rot.

The average thermal conditions in messes and work spaces are shown in detail. They approached, and in some cases exceeded, the accepted limits of effective temperature above which health and efficiency are likely to be impaired. The heat gained by air ventilating the ship's compartments ranged from 2-13 B.T.U./lb. of dry air. Further analysis showed that the high heat gains (4 B.T.U./lb. dry air) in two messes were caused to a large extent by inadvertent heating of the air while passing inwards through the supply duct.

The suggestion is made that the prevalence of the above skin diseases provides a useful indication of the severity of the thermal environment in ships.

[This valuable paper illustrates how one instrument, the sling psychrometer, may enable an extensive survey to be made of the thermal environment within compartments. Although this is the only instrument mentioned in the report, the author must have used a katathermometer or other instrument to measure air velocity. "Table I" at the foot of page 9 should read "Table II".]

M. L. Thomson

HADLER, W. A. Hematologia do pêñfigo foliáceo. [**Haematology of Pemphigus Foliaceus**] *Arquivos de Dermat. e Sifilografia de São Paulo.* 1949, 1950 & 1951, v. 13, Spec. No., 276 pp., 39 charts & 25 figs. [322 refs.]

In this monograph of over 250 pages, with 322 references and a considerable survey of the literature, the author describes a full haematological investigation of more than 300 cases of pemphigus foliaceus. The results are shown in very great detail in numerous tables, figures and photomicrographs and for an appreciation of the study, the monograph should be studied in the original. Among the important conclusions in respect of the disease itself, as distinct from alterations due to intercurrent factors (which he considers separately), the author notes a "chronic haemolytic syndrome", total leucocytosis with relative

and absolute neutrophilia and eosinophilia and a general leucocyte picture suggesting a chronic "toxi-infectious" process involving the reticulo-endothelial system. This process is also reflected in the bone-marrow picture, which shows a complex hyperplasia.

Readers of the Portuguese language will find a very full account of the changes described in this comprehensive study. [For earlier work on this subject by the author, see this *Bulletin*, 1948, v. 45, 464.]

H. J. O'D. Burke-Gaffney

VILLELA, E. Pinto y Pinta. [**Pinto and Pinta**] *Medicina*. Mexico. 1952, Jan. 25, v. 32, No. 644, 34-8. [Refs. in footnotes.]

The author discusses the similarities and the differences between *mal del pinto* as seen in Mexico and the pinta of Cuba. Discussion has been going on for some time as to whether these are identical or not. [If they are not, it is to be hoped that some name other than pinta will be found for the latter, for there will be endless confusion if two diseases are given names differing in one letter only.]

After many quotations and some discussion the author ends by presenting a useful table showing the chief differences between the endemic pinto (*mal del pinto*) of Mexico, Colombia, Brazil, Ecuador and Venezuela, the pinta of Cuba, and two other spirochaetal diseases, bejel ("Arabian syphilis") and yaws. The chief points in this table may be epitomized as follows:—

1. *Mal del pinto* (A) occurs in extensive endemic areas; Cuban pinta (B) in isolated cases; bejel and yaws (C) as isolated cases or small endemics.

2. Dyschromia generalized in A, often limited to hands and feet in B.

3. Palmar and plantar hyperkeratosis absent or very rare in A; is a dominant feature in B, very common in C.

4. Complement fixation absent in A; positive in 50 per cent. of B; variable and may be positive in C.

5. Aortitis has not been found beyond a doubt in A; subclinical aortitis present in 64 per cent. of cases of B (according to Pardo CASTELLO); present with varying frequency in C.

6. *Treponema carateum* has not been cultivated in A; positive cultures for treponemata have been obtained in B and in C.

7. Attempts at animal inoculation fail with A, nor are serological results obtained; scrotal inoculations in the rabbit produce in B lesion very similar to the initial sclerosis of syphilis; animal inoculation positive in C.

8. Experimental inoculation in man has reproduced the characters of A; LEÓN y BLANCO, in experimental work in Cuba with pinta, produced syphilis, contrary to all expectations.

H. Harold Scott

ANDLEIGH, H. S. **Rhinosporidiosis in Rajasthan. Report of Three Cases.** *Indian J. Med. Sci.* 1952, Jan., v. 6, No. 1, 16-22, 3 figs. on pl. [12 refs.]

"(1) Three cases of Rhinosporidiosis have been presented. Such cases have never before been reported from this part of the country.

"(2) All the three cases and the one already reported are males between the ages of 14-45 years. The left nostril in the three cases and right nostril in one case had been affected and the chronicity and slow-growing nature of the lesion is suggested from the clinical history of case 2. Except the nose, no other part of the body was involved in this series. Cases 1 and 3, however, suggest that the disease may develop rapidly.

"(3) In all the four cases a history of swimming associated with the onset of the disease has been elicited.

"(4) That excision is not the right type of treatment is evident from the previous case which was excised five times and case 2 which was once excised and yet the growth recurred.

"(5) It is interesting to note that we came across three cases of Rhinosporidiosis within the short period of 3 months. Rhinosporidiosis has not been reported from other northern provinces of India, and enquiries made suggest that Rhinosporidiosis does not occur in the U.P., etc. In this connection it will be interesting to note that one case of blastomycosis (Andleigh 1951) has been reported from Rajasthan."

NEGRONI, P., GATTI, J. C., CARDAMA, J. E. & BALIÑA, L. M. La blastomycosis sudamericana en la Argentina. A propósito de una observación. [**South American Blastomycosis in Argentina, with Observations on a Case**] *Rev. Argentina Dermatofilologia*. 1951, Oct.-Dec., v. 35, No. 4, 221-30, 4 figs. [50 refs.]

The following is a translation of the authors' summary :—

We present a new case of South American blastomycosis contracted in El Chaco and refer to 11 others hitherto unpublished.

Among 30 cases of this disease in Argentina, of which the source of infection could be determined exactly, we note that 17 lived in El Chaco, 6 in Misiones, 2 in Corrientes, 2 in Tucumán, 2 in Santiago del Estero and 1 in Formosa.

We hold strongly to our belief that this disease has a long incubation period, and that apparently autochthonous cases from other areas of the country have in fact acquired the infection in regions where South American blastomycosis is endemic.

H. J. O'D. Burke-Gaffney

TROPICAL OPHTHALMOLOGY

DODDS, G. E. **Blindness in Southern Nigeria.** [Memoranda.] *Brit. Med. J.* 1952, Mar. 15, 584.

The author investigated the causes of blindness in Southern Nigeria and bases his results on patients attending the Lagos Eye Clinic during the years 1946 to 1949. This clinic deals with 7,000 new cases and 20,000 attendances yearly and almost all the cases recorded were from Southern Nigeria.

The commonest causes of total blindness were cataract, glaucoma and optic atrophy. The author found 11 persons blind from the operation of couching for cataract.

In monocular blindness the sequence of frequency was cataract ; leucoma, phthisis and staphyloma ; trauma ; local infection ; iridocyclitis and glaucoma. Onchocerciasis was responsible for only one case of total and one case of monocular blindness. Trachoma was widespread but entropion was seen less in cases from Southern Nigeria than in cases from the Gold Coast and Northern Nigeria. Acute glaucoma was rarely seen.

The author is of the opinion that no single disease can be quoted as a main cause of blindness in Southern Nigeria.

The results are shown statistically in a table.

E. O'G. Kirwan

VARAS SAMANIEGO, J. M. **Ocular Manifestations of some Tropical Diseases.** *Amer. J. Ophthalm.* 1951, Nov., v. 34, No. 11, 1574-8.

The ocular manifestations of some tropical diseases in Ecuador are discussed by the author.

In malaria, which is endemic, ocular and periocular pains were constant symptoms; trigeminal neuralgia was of relative frequency and during the acute febrile period there was often a slight ptosis especially when the ocular pains were intense. He found that paralysis of the extrinsic muscles was very rare, but ciliary asthenopia occurred frequently during convalescence. In the febrile period there was marked hyperaemia of both the bulbar and palpebral conjunctivae. Herpes corneae occurred a few days after the temperature was normal, but considering the high incidence of malaria it was found to be a rare complication. He observed a few cases of complete blindness, but suspected that this was due to quinine intoxication rather than to malaria. In cases of hyperpyrexia, small interstitial haemorrhages were observed: these were quickly absorbed without leaving any residual defects.

American trypanosomiasis or Chagas's disease is endemic in Guayaquil; about 20 cases are seen annually. Almost all cases showed a unilateral oedema of the upper and lower eyelids as a result of the entrance of the parasite. There was also involvement of the bulbar conjunctiva manifested by oedema and due to the penetration of the mucosa by the parasite.

Amoebiasis is a widespread disease in Guayaquil, but the ocular manifestations were rare. The author has only seen one case of iridocyclitis and one of choroiditis which occurred during an attack of dysentery.

Ankylostomiasis is very prevalent in Ecuador. Bilateral oedema of the eyelids, paleness of the conjunctiva, greyish points on the sclera, pallor of the optic discs and changes in the vascular walls of the retinal blood vessels were the most common ocular manifestations in this disease. Ocular myiasis is rare and cases seen were caused by the *Dermatobia cyaniventris* or *D. hominis*. The larvae burrow beneath the skin causing cutaneous myiasis. The victims were young children. Various other insects are encountered, bites of which cause ocular disturbances, such as the Formicidia family, *Holeoponera whymperi*, *Poederos irritans* and the many varieties of bees, the most common being *Melipona flavipennis* and *Polistes versicolor*. The bites or stings of these insects often caused severe reactions in the lids, conjunctiva and cornea.

E. O'G. Kirwan

NACCACHE, R. **Clinical Trial of Aureomycin in Trachoma.** *Amer. J. Ophthalm.* 1951, Nov., v. 34, No. 11, 1591-3.

The author's results are based on the treatment of 35 cases of Trachoma I, II, III.

He used 1:1,000 aureomycin ointment (Lederle) as the most suitable medium and found that aureomycin is the best drug for the mass treatment of trachoma. It offers the following advantages: (1) low price, (2) no toxic effects, (3) rapid action on secondary infections and on complications, (4) sustained action on trachoma itself, (5) ease of administration.

E. O'G. Kirwan

TROPICAL ULCER

AMPOFO, O. & FINDLAY, G. M. **The Treatment of Tropical Ulcers with Aureomycin Ointment.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1951, Oct., v. 45, No. 2, 265-7.

The authors refer to their experience with aureomycin, by the mouth, with chloramphenicol and with terramycin in the treatment of tropical ulcer [this *Bulletin*, 1950, v. 47, 631; 1951, v. 48, 368; above, p. 625].

They then record the results with 12 children in the Gold Coast having tropical ulcers on the lower limbs who were treated with 3 per cent. aureomycin hydrochloride ointment applied locally on lint each day until healing occurred.

The results are shown in a table, which indicates that organisms disappeared from smears of the ulcer after 3-5 days' treatment. This was slower than when aureomycin was given by the mouth; yet the ulcers healed more rapidly than with any of the antibiotics given by the mouth. All of the ulcers had been present for at least a month and some reached 3-4 cm. in diameter but all were healed completely in 12-14 days.

It is suggested that the vitamin-like action of aureomycin may well provide a growth factor which is deficient in the devitalized tissues: local tissue nutrition is important in the production of tropical ulcer. One of the authors, in unpublished experiments, showed that if an intradermal auto-inoculation of pus was made over the fleshy part of the gastrocnemius muscle in a patient with tropical ulcer, a small sore formed which healed rapidly. A similar inoculation over the skin of the external malleolus was followed by the development of a rapidly spreading ulcer, with abundant fusiform bacilli and spirochaetes.

The disadvantage of local application of aureomycin is the necessity for daily changing of dressings, but on the other hand, oral administration is not easy in young children. In the local treatment, toxic reactions are avoided and the rate of healing is increased.

H. J. O'D. Burke-Gaffney

LASBREY, A. H. **Tropical Ulcers of the Leg and Nail Bed. Aureomycin Ointment in their Treatment.** *South African Med. J.* 1952, Jan. 26, v. 26, No. 4, 66-9, 2 figs.

Tropical ulcers are often seen in Africans, especially children, in Durban. The lesion is usually small, but painful and persistent. The author reports on 74 cases in which a dramatic response resulted from treatment with aureomycin ointment. Not one failed to show immediate response and 34 returned to show completely epithelialized ulcers.

The patients were young Bantus, between 8 and 20, living under poor conditions outside Durban. Sixty ulcers were on the leg or foot and 14 on the nail-bed of the toe. The author describes the nail-bed tropical ulcer, as it is not often recognized. It is circular or oval, $\frac{1}{4}$ -1 inch in diameter, slightly raised, with a sero-purulent, greyish-green discharge, often sanguineous. The surface is commonly covered with discharge and encrusted dirt and the base unhealthy, pale and having irregular granulation and sloughs. The odour is often offensive. The proximal end is bounded by the necrotic remnant of the nail. The terminal phalanx is usually swollen to one and a half times its normal size. Pain is severe. Photographs illustrate nail-bed ulcers before and after treatment.

Eleven nail-bed ulcers were swabbed before treatment and spirochaetes and fusiform bacilli were found in 10. In 35 ulcers of the leg or feet, spirochaetes were found in 26 and fusiforms in 31. Culture revealed a variety of cocci and sometimes diphtheroids: in only one case were spirochaetes or fusiforms isolated after the first application of aureomycin. A case is described in which a large ulcer was examined after the initial dressing. Before application of aureomycin, the usual flora was present and this included coagulase-positive staphylococci and non-haemolytic streptococci. Fusiform bacilli persisted for 24 hours after the dressing, but after 36 hours, no organisms were seen or isolated. In 26 cases the Wassermann reaction was done and in 3 it was positive. Healing was not delayed in these cases.

Treatment consisted in wiping away discharge with a saline or eusol swab, wiping the base of the ulcer with a dry swab and applying aureomycin ointment sparingly on dry gauze. A small pad of cotton wool and a gauze bandage were applied, and no other treatment was given. Necrotic remnants of toenails were not removed. Patients were asked to return for dressing every 5 days, but in practice the intervals varied between 3 and 14 days.

For ulcers varying from $\frac{1}{2}$ to $2\frac{1}{2}$ inches in diameter a $\frac{1}{2}$ oz. tube of aureomycin lasted for about 30 dressings. The cost of each dressing was therefore slightly more than 3 pence.

Two tables give full details of 21 patients with leg or foot ulcers and 9 with nail-bed ulcers, who returned to show complete healing. Of the 30, 13 were epithelialized in a week and 7 more within 2 weeks. They had been present for a week to a year. The number of dressings varied from 1 to 7 and often did not exceed 2 or 3. Many patients reported a marked relief of pain within 48 hours of the first application of aureomycin.

When the first dressing was removed (usually after 5 days) the discharge was no longer offensive, the dressing did not adhere to the surface and its removal was painless. The surface was clean, with healthy granulations, often with ingrowing epithelium. Heaped-up edges had flattened and depth had decreased.

Four illustrative cases are described in detail.

The author discusses the use by other workers of aureomycin and other antibiotics in the treatment of tropical ulcers. Special reference is made to the work of AMPOFO and FINDLAY who used oral aureomycin [this *Bulletin*, 1951, v. 48, 368]. The present author considers that the rates of healing were comparable but, while aureomycin capsules for oral use have obvious advantages in rural Africa, this method is more expensive at present and introduces "the undesirability of giving a potent antibiotic which is as effective when used locally". He also refers briefly to the treatment with dried yeast described by HALLINAN [wrongly referred to throughout as "HALLIMAN"], but in these cases healing seemed to be slower [*ibid.*, 1950, v. 47, 885].

The author concludes that the method described by him constitutes a simple, effective, inexpensive, ambulant treatment for the smaller tropical ulcer.

H. J. O'D. Burke-Gaffney

See also p. 625, AMPOFO & FINDLAY, **Terramycin in the Treatment of Yaws and Tropical Ulcer.**

PROTOZOOLOGY : GENERAL

FISHER, O. D. **Toxoplasma Infection in English Children. A Survey with Toxoplasmin Intradermal Antigen.** *Lancet.* 1951, Nov. 17, 904-6. [10 refs.]

The author reports the results of a survey of the incidence of toxoplasmosis among English children, in whom the intradermal test was used for diagnosis. The antigen (known as "toxoplasmin"), obtained from the peritoneal fluid of infected mice, was prepared by FRENKEL's method [this *Bulletin*, 1949, v. 46, 402]. The dose for the test was 0.1 ml. of 1/500 toxoplasmin, which was injected intradermally, while antigen prepared from normal mouse spleen was used for control animals. The reaction, which was observed 1, 2 and 3 days later, was found to reach its maximum after 48 hours. The response was assessed from the size of erythema and induration appearing at the site of injection.

In one series, 639 mentally defective children at a London hospital were tested with toxoplasmin, and the results were checked by serological methods (dye-test and complement-fixation test). In addition to these, 59 adults from the same hospital were tested.

The incidence of infection in the 0-4 years age-group (186) was insignificant (below 1 per cent.), in the 5-9 years group (322) it was 4.3 per cent., and in the 10-14 years group (216) 7 per cent., while in adults (upwards of 15 years : 177 patients) the reaction was positive in 17.5 per cent.

It is concluded that the toxoplasmin intradermal test represents a reliable method for detecting toxoplasmic infection in population surveys and in suspected clinical cases.

C. A. Hoare

CHRISTEN, R., AGOSIN, M., PINO, F., JARPA, A., THIERMANN, Erica & NEGHEM, A. Primer caso confirmado de toxoplasmosis humana en Chile. Comunicación preliminar. [First Confirmed Case of Human Toxoplasmosis in Chile. Preliminary Note] *Rev. Med. Chile.* 1951, Nov., v. 79, No. 11, 714-15, 1 fig.

OTTEN, E., WESTPHAL, A. & KAJAHN, Elisabeth. Über das Vorkommen von Toxoplasmose beim Hunde. Statistische Erhebungen. [Occurrence of Toxoplasmosis in Dogs. Statistical Data] Reprinted from *Monats. f. prak. Tierheilk.* 1950, v. 5, No. 2, 305-8. [10 refs.]

Among the numerous animals harbouring *Toxoplasma*, the dog has attracted particular interest as a possible reservoir of human infection in view of its close association with man. Since much of the previous evidence on this question is circumstantial, the authors have carried out a systematic investigation of the incidence of toxoplasmic infection among dogs in Hamburg. Sabin-Feldman's dye-test was applied to 84 samples of blood from dogs varying in age from foetus to adults up to 13 years old, belonging to each sex and 14 different breeds. Thirty animals reacted positively to titres from 1 : 25 to 1 : 800 ; in 7 out of 35 animals a latent infection was detected. Among 13 dogs (out of 26) showing symptoms of toxoplasmosis, a number were suffering from encephalitis and neuritis, while in 7 out of 15 dogs suffering from diarrhoea the dye-test was positive. It was also positive in a bitch which had an abortion and in two dogs with myalgia. There was no evidence of any influence of age, sex or breed on the incidence of infection.

C. A. Hoare

BLANC, G., BRUNEAU, J. & CHABAUD, A. Quelques essais de transmission de la toxoplasmose par Arthropodes piqueurs. [Transmission of Toxoplasmosis by Biting Arthropods] *Arch. Inst. Pasteur du Maroc.* 1951, v. 4, No. 4, 298-303.

With a view to determining the rôle of blood-sucking arthropods in the transmission of toxoplasmosis, the authors carried out experiments with fleas (*Xenopsylla cheopis*), Diptera (*Stomoxys calcitrans* and *Aedes aegypti*) and ticks (*Rhipicephalus sanguineus*), on the one hand, and rodents (mice, guinea-pigs, ground squirrels), on the other.

It was found that all these arthropods could be readily infected by feeding them on infected ground squirrels (*Xerus*). However, the arthropods remained infective to the rodents only for several hours after the infecting feed, for all attempts to transmit the infection later failed. The positive results were obtained by inoculation of the material from infected arthropods, whereas attempts to transmit the infection through the bite were in all cases unsuccessful. All the rodents refractory to infection by arthropods were afterwards successfully infected by the syringe, with a passage strain of *Toxoplasma*.

C. A. Hoare

BLANC, G. & BRUNEAU, J. Préparation d'un sérum animal neutralisant le virus de la toxoplasmose. [**Preparation of Animal Serum for the Neutralization Test in Toxoplasmosis**] *Arch. Inst. Pasteur du Maroc*. 1951, v. 4, No. 4, 291-7, 2 figs.

This paper, which has also appeared elsewhere, has already been reviewed in this *Bulletin*, 1951, v. 48, 202.

WESTPHAL, A. & SCHULTZ, W. Die klinische Bewertung der Titer beim Sabin-Feldman-Serofarbstofftest auf Toxoplasmose. [**Clinical Value of the Titre in Sabin-Feldman's Dye-Test for Toxoplasmosis**] Reprinted from *Ztschr. f.d. ges. Innere Med. u. Grenzgebiete*. 1950, v. 5, Nos. 23/24, 761-5.

In view of the variability of the titre of sera in the dye-test for toxoplasmosis, the authors have set out to determine standards which would be of diagnostic value when tested with the strain of *Toxoplasma* used in Germany (Bk). For this purpose, titres of 1 : 4, 1 : 25, 1 : 50, 1 : 100, 1 : 200, etc., were employed, and the tests were carried out on mothers who had had normal deliveries, on women who had had stillbirths, and on clinical patients with encephalitis, ocular lesions and other symptoms of toxoplasmosis. The findings, which were confirmed by animal experiments, indicated that a titre of 1 : 4 could be regarded as negative, whereas titres of 1 : 50 and higher were positive beyond doubt. As regards 1 : 25, in many instances this titre corresponded to clinically positive cases, while in others a non-specific reaction could not be excluded. However, on the basis of experimental infections, it would seem that the latter might represent those recovered from the infection, on account of which the reaction can also be regarded as positive. In doubtful cases, reacting to a titre of 1 : 25, the test should, therefore, be repeated.

C. A. Hoare

ENTOMOLOGY AND INSECTICIDES : GENERAL

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

RICHARDS, A. G. **Studies on Arthropod Cuticle. VII, Patent and Masked Carbohydrate in the Epicuticle of Insects.** *Science*. 1952, Feb. 22, 206-8, 7 figs.

MATTINGLY, P. F., ROZEBOOM, L. E., KNIGHT, K. L., LAVEN, H., DRUMMOND, F. H., CHRISTOPHERS, S. R. & SHUTE, P. G. **The *Culex pipiens* Complex.** *Trans. Roy. Entom. Soc. of London*. 1951, Nov. 21, v. 102, Pt. 7, 331-82, 5 figs. [Numerous refs.]

[This is a series of short papers, introduced by Mr. Mattingly on various aspects of the *Culex pipiens* complex. Most of the papers deal with detailed relations between pairs of forms; either *pipiens-fatigans* or *pipiens-molestus*. The following abstract attempts to summarize the subject in a general way.]

The main forms.

The three most important types of the *Culex pipiens* complex are: *C. pipiens* described by LINNAEUS from N. Europe in 1758; *C. molestus* by FORSKÅL from Egypt in 1785 (sometimes described as *C. autogenicus*); and *C. fatigans* by WIEDEMANN from the East Indies in 1828. American writers prefer to call the last *C. quinquefasciatus* Say.

In addition to these main forms there are varieties such as *pallens* (= ? *comitatus*) and *dipseticus*. These are intermediate morphologically between *pipiens* and *fatigans* and they occur in regions of overlap of those forms. Since crossing of the two types has been demonstrated in the laboratory with the production of intermediate forms, there is reason to believe that these varieties may merely be naturally occurring hybrids.

Distribution.

The *pipiens* form is holarctic, extending down to latitude 30 or 40°N. ; there is also an extension down East-central into South Africa. There is also an isolated zone of *pipiens* in Argentina, probably arising from an introduced population.

C. molestus occurs in a large part of the *pipiens* area, i.e., West and Central Europe, the Near East, North Africa and the Sudan. It appears to be widely distributed in the U.S.A. An isolated zone (? introduced) has been observed in Eastern Australia.

C. fatigans is cosmopolitan. It overlaps with *pipiens* along the latitude 40°N. in U.S.A., in Irak and Persia and in China. In the overlap zone in China and U.S.A. occur the forms which are thought to be hybrids.

Morphological differences.

Some of the more important differences between the 3 forms may be summarized thus :—

	<i>pipiens</i>	<i>molestus</i>	<i>fatigans</i>
male phallosome	Dorsal processes only slightly divergent		Dorsal processes widely divergent
Ratio : length of anterior fork cell on wing to its petiole	>3		<3
male palpi	longer than proboscis	about as long as proboscis	
siphonal index of larva	5 or more	about 4	

In addition to these points, *pipiens* is generally darker than *molestus*, and has patches of dark scales on the abdominal sternites which are very inconspicuous in typical *molestus*.

Comment.—The only one of all the above characters which seems to be reliable is the form of the male phallosome which differentiates *fatigans*. The other characters are too variable to be relied upon to distinguish individual specimens.

Biological differences.

These may be summarized as follows :—

	<i>pipiens</i>	<i>molestus</i>	<i>fatigans</i>
1.	anautogenous	autogenous	anautogenous
2.	eurygamous	stenogamous	stenogamous
3.	not man-biting	man-biting	man-biting
4.	hibernates	does not hibernate	does not hibernate

Comments.

1. *Autogeny* (the power of laying eggs without a blood meal).—*Molestus*, though it will readily suck blood if opportunity arises, can lay a batch of eggs before taking blood ; for further batches, blood meals are required. Autogeny is inherited. In crosses between *molestus* and *pipiens* the appearance of autogeny is delayed until the F_2 generation (recessive). Strains of *pipiens* reared from wild specimens often produce some offspring capable of autogeny. This suggests that *pipiens* and *molestus* interbreed in nature.

2. *Stenogamy*.—The ability to breed in small spaces (stenogamy) is an important character differentiating *molestus* from *pipiens*. *Molestus* will breed in a cage as small as 3 cubic inches in contrast to *pipiens* which requires, as a minimum, a cube of about 14 inches.

3. *Man-biting*.—Choice of host is not absolutely rigid. It seems that *pipiens* and *molestus* both prefer to bite birds ; but whereas *molestus* will bite man as an alternative, *pipiens*, in general, will not. It should also be noted that *fatigans* will not always bite man, as certain W. African strains which have been colonized at Dakar refuse to do so

4. *Hibernation*.—The failure of *molestus* to accomplish gonotrophic dissociation and hibernate, probably accounts for its absence from the more northerly parts of Europe and its greater prevalence in the Mediterranean region. This character, together with stenogamy and man-biting, probably accounts for the frequent occurrence of *molestus* in towns rather than rural areas in northern regions. It has often been recorded breeding in underground cellars, etc., in London, for example. It has been pointed out, both in Germany and in California, that there appear to be clines of the *pipiens* complex, with greater concentration of the *molestus* type (with autogeny) in southern regions.

Hybridization.

Careful American work has shown that typical *pipiens* and *fatigans* can be crossed in the laboratory, in both directions, and the hybrids can be maintained breeding vigorously for 11 generations. A number of investigators have also crossed *molestus* and *pipiens* and shown something of the genetic nature of autogeny and stenogamy. Strains of *molestus* and *fatigans* have been crossed in California.

The existence of intermediate forms between *pipiens* and *fatigans* in zones of overlap suggests that these forms hybridize in nature. The sharing of the gene for autogeny is similar evidence for *pipiens* and *molestus*.

Conclusions.

It has been suggested that the *pipiens-fatigans-molestus* complex represents a cosmopolitan polytypic species. Local climatic conditions favour the emergence of types with certain combinations of biological characters. These combinations are far from rigid and sometimes, for example, stenogamy or eurygamy were not correlated with feeding on mammal or bird blood. Nevertheless, under "typical" conditions (at the end of a cline) typical forms of *pipiens*, *molestus* or *fatigans* are likely to be found, probably with associated morphological characteristics.

Against this, there is some evidence of genetical differentiation within *molestus*, resulting in reproductively incompatible strains. J. R. Busvine

GEORGOPOULOS, G. [On the Effects of Insecticide Chlordane (Octa-Clor) on the House Fly (*Musca domestica* L.)] Arch. Hyg. Athens. 1951, Jan.-Apr., v. 4, Nos. 1/4, 108-19, 1 map & 2 charts. [12 refs.] [In Greek.] English summary.

This paper is written in modern Greek, but the author's summary in English states that in May 1951 all the houses in 5 villages in Attica were sprayed

either with Chlordane alone (1.48 gm./metre) or Chlordane with DDT (1.40 gm. Chlordane and 0.5 gm. DDT per metre). Three comparable villages were used as controls. Inspections were made until the end of September. Results were equally satisfactory whether Chlordane was used alone or with DDT. House-flies disappeared completely from the sprayed villages on the 4th or 5th day after spraying and remained absent throughout the entire season (May–October).

The cost per head was lower for the combined spraying than for large-scale DDT spraying, but was slightly more than the use of Chlordane alone. The original text contains 5 tables, 1 figure and a sketch-map of the area studied.

H. J. O'D. Burke-Gaffney

TRAUB, R. & JOHNSON, Phyllis T. **Fleas collected during a Plague Survey in Venezuela.** *Bol. Oficina Sanitaria Panamericana.* 1952, Feb., v. 32, No. 2, 111–35, 35 figs. on 10 pls.

FERRIS, G. F., with Chester J. STOJANOVICH. **The Sucking Lice.** *Memoirs Pacific Coast Entom. Soc.* San Francisco. 1951, Oct., v. 1, pp. ix+320, 124 figs. [40s.]

BARNETT, H. C. & KNOBLOCK, E. C. **Chemical and Biologic Studies on DDT Resistance of Lice.** *U.S. Armed Forces Med. J.* 1952, Feb., v. 3, No. 2, 297–304. [Refs. in footnotes.]

This work, on lice from Tokyo, confirms the observations of HURLBUT *et al.* [this *Bulletin*, 1952, v. 49, 565] by additional tests. Also, the lice could be killed by 6 alternative insecticides, which were based on gamma BHC, on pyrethrum and on allethrin.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

BULL. WORLD HEALTH ORGANIZATION. Geneva. 1952, Suppl. 3. **Medical Certification of Cause of Death. Instructions for Physicians on Use of International Form of Medical Certificate of Cause of Death.** 20 pp. [1s.; \$0.20; Sw. fr. 0.75.] [Summary appears also in *Bulletin of Hygiene*]

The International Form of Medical Certificate of Cause of Death designed by the Sixth Decennial International Revision Conference in 1948 and recommended by the World Health Organization for use by member states provides for the statement of :—

- I. The disease or condition directly leading to death, together with such antecedent morbid conditions as may exist, so that the underlying cause of death will be clearly indicated, and
- II. Such other significant conditions contributing to the death but not related to the disease or condition causing death.

The use of the International Certificate places upon the certifier the responsibility of indicating the sequence of events so that the underlying cause of death can be readily identified by the statistical office, the underlying cause being defined as :—

- (a) The disease or injury which initiated the train of morbid events leading directly to death, or
- (b) The circumstances of the accident or violence which produced the fatal injury.

It is a new principle in the mortality statistics of most countries that assignment should be to the underlying cause of death as indicated by the certifier, rather than to one or other of the conditions mentioned on the certificate in accordance with fixed rules of precedence and without regard to the order of statement.

The booklet describes the structure of the death certificate and explains, with a series of informative examples, how the various conditons leading to death should be stated. The direct cause of death, to be entered in line I (a) "does *not* mean the mode of dying (e.g., heart failure, respiratory failure), which should not be stated at all since it is no more than a synonym for the fact that death occurred and provides no useful information". In regard to antecedent causes, to be entered in lines I (b) and (c), "hypothetical constitutional states or factors which may have preceded, or predisposed to, a well-defined disease should not be entered as antecedent cause". Advice is also given on the proper way to complete Part II (other significant conditions) and the column for statement of interval between the onset of each condition and death.

The certifying physician is sometimes uncertain about how much detail of cause of death he is expected to give, but failure to give sufficient information to permit of precise classification in accordance with the International List leads either to the sending of enquiries or, if this is not done, reduces the quality and usefulness of the mortality statistics. Advice is given on the principal deficiencies found on death certificates and how they can be avoided, with numerous examples of terms requiring qualification or elaboration. A 5-page annex lists 120 examples of incomplete descriptions of cause of death, indicating the additional information needed for satisfactory coding according to the International Classification.

[This is a most valuable booklet which will not only help practising physicians and pathologists, but will provide useful information to teachers and to Public Health officials who seek an understanding of the principles of death certification. The International Form of Death Certificate is now in use in England and Wales, Northern Ireland, the Irish Republic, and many other countries. It is not used in Scotland.] *W. P. D. Logan*

COONOR. **The Pasteur Institute of Southern India, Coonoor. Annual Report of the Director, together with the Forty-Fourth Annual Report of the Central Committee of the Pasteur Institute Association 1950-51 and Scientific Report 1951.** 59 pp., 1 chart. 1952. Madras: Diocesan Press.

This report gives the usual full statistical account relating to anti-rabic treatment at the Institute and its Centres. It is noted that during the year there were 306 persons fully treated at the Institute (299 Asians, 7 Europeans) with 2 deaths; and 8,271 (8,134 Asians and 137 Europeans) in subsidiary centres with 20 deaths, giving death rates of 0.65 and 0.24 respectively.

General laboratory examinations amounted to 4,938. Reports are given of special investigations and these include a study of biochemical changes in sheep inoculated with fixed rabies virus, by BALASUBRAMANIAN and AJJAH. The only significant variation was a hyperglycaemia usually beginning on the 5th or 6th day and increasing thereafter.

MENON and SUKUMARAN compared several serological methods and antigens for the diagnosis of syphilis and record their results in detail. The impression gained was that cardiolipin antigens were superior, especially in eliminating false positive reactions. KURIAN and Sukumaran used this antigen in complement-fixation tests of 181 sera from leprosy patients, comparing them with

W.R. and Kahn tests. There were 17 positive with the cardiolipin, 67 with the W.R. and 80 with the Kahn test. As this was the reverse of the finding of Ross and GEMAR at Carville [this *Bulletin*, 1950, v. 47, 1000] which was attributed to intensive sulphone treatment, the present authors tested 18 sera from leprosy patients thus treated. All were negative to complement-fixation tests with cardiolipin antigen before sulphone treatment, but after treatment 4 became positive.

Kurian describes a laboratory study of enteric fever in the Nilagiri District and Menon a familial sex-linked bleeding diathesis. Menon also describes a detailed study of influenza, from the W.H.O. Influenza Centre at the Institute, and gives a brief description of *Staph. aureus* and haemagglutination of fowl cells.

The Report includes the usual administrative and financial information. [For the 1949-1950 report see this *Bulletin*, 1951, v. 48, 599.]

H. J. O'D. Burke-Gaffney

WATSFORD, S. D. **Medical Services to Natives in the Northern Territory.** *Health.* Canberra. 1951, Dec., v. 1, No. 4, 8-10.

The author, who is Deputy Director of Health in the Northern Territory of Australia, describes the medical care provided for that large area by the Commonwealth Department of Health.

The Northern Territory is inhabited by some 14,500 indigenous people, about half of whom occupy the tropical monsoon area above the 18th parallel and the remainder live in the Barkley Tablelands and in the arid regions of Central Australia. The native types vary from the semi-civilized who live near the large cattle stations and larger townships to nomads in the desert or in the Arnhem Land Native Reserve who have little contact with white civilization. Those in the northern half are prone to acquire such tropical diseases as leprosy, hookworm, and malaria, while in the dry southern half trachoma is prevalent although it is unknown in the tropical north.

The free medical service provided includes hospital facilities and transport by road or air when necessary. Native wards are found in the hospitals at Darwin, Alice Springs, Katherine and Tennant Creek and they are usually the same as those provided for white patients. During 1950-1951, the daily averages in them have been respectively 35, 35, 9 and 4.

In addition, many of the people are treated in their own tribal country at Government and Church Missions and at cattle stations. Free medical kits, amounting to over 300, are provided and maintained and these vary from fairly extensive equipment at Missions to simple first-aid kits for small stations. Some of the Church and Government Missions have sick quarters and trained sisters are in charge of 15 of them. Most of these units are in daily radio communication with Darwin or Alice Springs and treatment is often prescribed over the radio. If necessary a doctor or sister is flown to the spot and in the last year 97,000 miles were flown in such emergency calls, most of them on behalf of the native people.

As many missions as possible are visited regularly. The stations around the Arnhem Reserve are visited every month: some 7 or 8 missions are visited and this involves a flight of 960 miles. The visits are announced in advance by radio. These trips last for 2 or 3 days and as many as 150 people may be examined. One medical officer is employed solely on extensive surveys of these stations, where he is flown and remains for 3 or 4 weeks, examining all the indigenous people in the area and recording results. In this way, the incidence of such conditions as leprosy, malaria, yaws, granuloma and hookworm are fairly accurately determined. In a short time the records of the

state of health of some 3,000 people have been compiled and filed. Advice on health and sanitation is given in all areas.

The author refers to the difficulties attached to dealing with these primitive people : these will be only too familiar to medical workers in tropical countries. The nomads and even some of the more civilized tribesmen will often avoid the doctor and will not come to hospital : reliable histories are few : stay in hospital is disliked and many people abscond : isolation is difficult and even those who improve in hospital often relapse into the practice of herding together in unhygienic conditions when they return to their tribal surroundings.

"The general health of the natives in the Northern Territory leaves much to be desired." Most of those in the northern half have hookworm and the incidence of leprosy is stated to be the highest in the world. Tuberculosis is spreading because of bad hygienic conditions and difficulties of treatment. The common childhood diseases occur in frequent epidemics, with high mortality rates, even in adults. Nevertheless the people have a high resistance to many other diseases : the author cites 5 cases of suppurative arthritis of the knee joint which were completely restored to normal after aspiration and penicillin therapy. Similarly, recovery often occurs in an amazingly short time from gross injuries and burns.

It is encouraging to record that "the value of white man's medicine is being appreciated and the policy of consideration and persuasion rather than force or discipline is paying dividends". Experience has shown—as it has so often elsewhere—that if, for example, an infective leprosy patient is removed from an area against his or his tribe's wish, nobody can be found the next time the doctor visits that area. The best ambassadors of the medical service are often those who have been treated as equals in the Northern Territory hospitals and who "have been shown that certain sections of the white community are interested in their welfare".

The success of the medical services naturally depends on the co-operation of missionaries, Native Affairs Officers and cattle station managers. This is often freely given, but much work will be required to improve the health of the native peoples, if their welfare is to be assured and their gradual assimilation into our more civilized conditions is to be achieved.

H. J. O'D. Burke-Gaffney

POLSKIE TOWARZYSTWO PARAZYTOLOGICZNE [Polish Parasitological Society].

Pamiętnik II Zjazdu Polskiego Towarzystwa Parazytologicznego w Puławach 10–11 VI 1950. (*Proc. II Meeting Polish Parasitological Soc., Puławy, 10–11 June, 1950*) Gdańsk. 1950. 140 pp.

This report is published in Polish, but there are brief summaries in English of the subjects dealt with.

Those of direct interest to readers of this *Bulletin* include an account of 5 cases of cysticercosis of the brain in 5 of 1,548 dogs, accompanied by rabies in one case ; the presence of *Fasciola hepatica* in 18 calves less than 3 weeks old : investigations of the annual cycle of the *A. maculipennis* population in Danzig, from which it is noted that 3 generations of *A. m. atroparvus* are hatched per year : dependence of fertility of female *A. m. atroparvus* on their age : presence of *Enterobius* in 90 per cent. of children examined in Danzig, and its treatment : the presence of *Enterobius* (up to 20 or more in number) in 25 of 60 operated appendices : and success with local preparations of DDT in campaigns against flies.

H. J. O'D. Burke-Gaffney

MACKAY, D. H. **Skeletal Maturation in the Hand : A Study of Development in East African Children.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1952, Mar., v. 46, No. 2, 135-50, 1 map & 38 figs. on 21 pls.

"A radiological investigation of the ossification and maturation of the carpal bones in 1,360 East African children of known ages has been described.

"The work has revealed that there is no difference in the order of appearance of the carpal ossification centres from that commonly accepted for other races. The fact that skeletal maturation is more rapid in girls than in boys has been confirmed.

"The rate of skeletal maturation has been compared with findings of other writers on American children, and the African children investigated have been found to be from $1\frac{1}{2}$ to 2 years behind present American standards."

The West African Medical Journal

In March, 1952, there appeared the first issue of this journal to be produced since 1938, when publication ceased after the journal had been in existence since 1927. The new series is published under the auspices of the Directors of Medical Services of Nigeria, Gold Coast, Sierra Leone and Gambia, and it is edited by Dr. D. B. Jelliffe, from University College, Ibadan, Nigeria.

The Bureau of Hygiene and Tropical Diseases offers a cordial welcome to this journal, in its new lease of life.

Charles Wilcocks

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